ARCHIVES of OPHTHALMOLOGY

VOLUME 8 (old series Volume 65) SEPTEMBER, 1932 NUMBER 3

RESECTION OPERATION FOR STRABISMUS

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The resection operation for strabismus is presented for the following reasons:

1. In employing the Reese resection two stitch infections occurred, and several infections have been seen following the operation by other surgeons. Three causes for these infections other than lack of sterile technic may be: (*a*) the position and closure of the conjunctival wound, (*b*) the manner in which the sutures are inserted and (*c*) the prolonged bandaging after operation.

2. With the Reese technic the resulting scar is often slightly disfiguring, and granulating wounds are frequently encountered. The position of the conjunctival wound and the suturing technic may be partially responsible for these disadvantages.

3. It seems advantageous to review the indications for the resection operation in the light of the newer operations of recession [1] and retroplacement [2] and the older operation of advancement.

4. The technic of resection, described in detail here and previously [2a] outlined, has now been used for eight years with excellent results and no complications.

The technics for resection most widely known in North America include those of Schweigger,[3] Reese,[4] Lancaster [5] and Wilkinson.[6] These

1. (*a*) Curdy, R. J.: Operative Treatment of Squint, J. Missouri M. A. **13**:16, 1916. (*b*) Jameson, P. C.: The Principles of Muscle Recession with Scleral Suturing as Applied in the Correction of Squint, Tr. Ophth. Soc. U. Kingdom **45**:405, 1925; (*c*) The Surgical Entity of Muscle Recession, Arch. Ophth. **6**:329 (Sept.) 1931. (*d*) Agatston, S. A.: Muscle Retroplacement in Conditions of Squint, Am. J. Ophth. **7**:361 (May) 1924.

2. (*a*) Berens, C., in discussion on Jameson (footnote 1 *b*, p. 415). (*b*) Berens, C.; Losey, R. R., and Connolly, P. T. Retroplacement for Strabismus, Am. J. Ophth. **12**:720 (Sept.) 1929.

3. Schweigger, C.: Die Erfolge der Schieloperation, Arch. f. Augenh. **29**:165, 1894.

4. Reese, R. G.: A New Muscle Resection Operation for Squint, New York State J. Med. **45**:60 (Jan. 13) 1912.

technics and several other methods may be visualized by referring to figures 1 and 2. Lancaster's technic [5] seems to be free from most of the objections raised. The differences between his method and the technic to be described are indicated in figures 1 and 2. My technic differs slightly from the operation devised by Lancaster,[5] in which two mattress sutures are used. Posey [7] has also found the use of two double-armed sutures of value in the advancement operation. An ingenious technic devised by Castresana [8] combines resection with stretching of

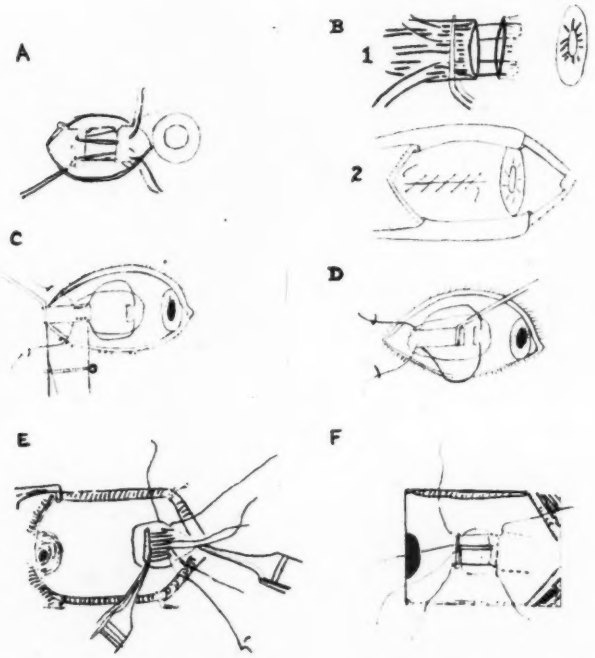

Fig. 1.—*A*, Schweigger's resection operation for strabismus. *B*, Lancaster's resection operation for strabismus: *1*, muscle held in normal position, showing position of sutures; *2*, conjunctiva closed by a running continuous suture which need not be tied. The dotted lines show the site of the buried sutures. If a tuck is made the fold is also buried. *C*, resection operation (Wilkinson). *D*, resection operation: suture in place and muscle held back to original position (Wilkinson). *E* and *F*, resection operation (Reese).

5. Lancaster, W. B.: A Satisfactory Operation for Muscle Shortening or Advancement, Am. J. Ophth. **1**:161 (March) 1918; Operation to Shorten a Rectus Muscle with Buried Sutures, Am. J. Ophth. **14**:483 (June) 1931.

6. Wilkinson, O.: Present-Day Status of Squint Surgery: A New Operative Technic, Tr. Sect. Ophth. A. M. A., 1922, p. 310.

7. Posey, W. C.: The Muscle Advancement Operation: A Twin Single Stitch Method, Tr. Am. Acad. Ophth., 1921, p. 83.

8. Castresana, B.: Nuevo tratamiento quirúrgico del estrabismo, Internat. Cong. Ophth., Washington, D. C., 1922; Am. J. Ophth. **5**:669 (Aug.) 1922.

the antagonistic muscles. He tenotomizes the tendon and passes three single-armed sutures through the conjunctiva, the stump and the episcleral tissue, and then through the muscle and conjunctiva. The episcleral sutures form a rhomboid, and he believes that he can correct cyclotropia by tightening one of these sutures more than the others (fig. 3). A simplified technic has recently been published by Agatston.[9]

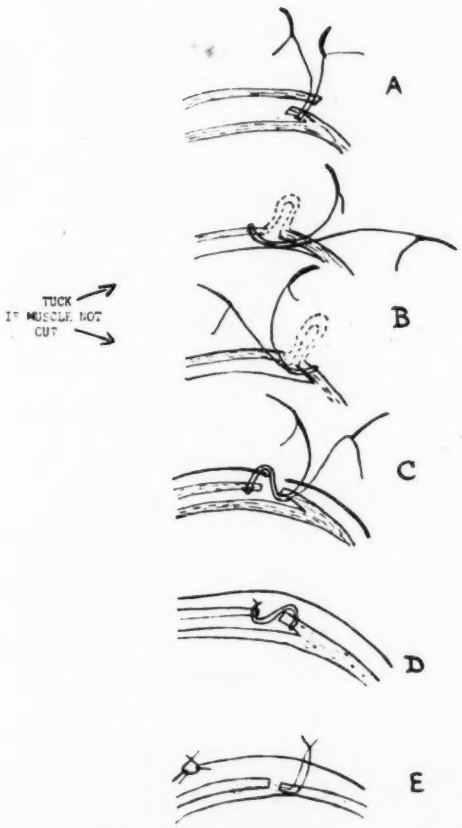

Fig. 2.—Methods used by various ophthalmic surgeons when inserting the mattress suture through the tendon stump, conjunctiva and muscle in the resection operation. (Modified from Lancaster.) *A*, method of resection of Snellen, 1869; Ewing, 1915; Lancaster, 1918; Duverger, 1919; *B*, that of Butler, 1916; Fromaget, 1921; *C*, that of Noyes, 1874; Reese, 1912; *D*, method of Lancaster, 1931; *E*, method of Berens, 1925.

AUTHOR'S PROCEDURE FOR RESECTION

Preliminary Examination.—Before operation a careful general physical examination is always made; the degree of strabismus is repeatedly

9. Agatston, S. A.: A Simplified Method of Muscle Resection for Squint, Am. J. Ophth. **14**:1144 (Nov.) 1931.

checked by several observers, and correction of the deviation by means of lenses and orthoptic training is usually attempted.

Instruments for Resection.—These are as follows:

1 Eye speculum
2 Fixation forceps with catch
2 Fixation forceps without catch
2 Mouse-tooth forceps
1 Clot forceps
1 Prince forceps
2 Strabismus hooks
1 Tenotomy scissors
1 Stevens scissors
1 Needle holder
3 Suture clips (Luer)
1 Calipers
1 Millimeter rule
2 Double-armed no. 3 twisted, paraffinized black silk sutures (000-10 day catgut may be used)
1 Single-armed no. 3 twisted, paraffinized black silk suture (000-10 day catgut may be used)
1 Single-armed no. 1 twisted, paraffinized black silk suture
6 Needles (3/8 circle; no. 5—Berbecker, England)

TECHNIC OF OPERATION

First Stage.—Insertion of traction suture and conjunctival incision. Sutures of no. 3 twisted, paraffinized black silk (fig. 4) are inserted to expose the internal or external canthus, respectively. The insertion of the muscle to be resected is exposed by a curved conjunctival incision 12 mm. in length, with the concavity toward the cornea, as close as possible to the semilunar fold in operations on the internal rectus, and close to the external canthus in operations on the external rectus. The conjunctiva is carefully dissected toward the cornea until the muscular insertion is completely exposed (fig. 5).

Second Stage.—Isolation of the muscle. Tenon's capsule is seized well below the insertion of the muscle with straight forceps and incised with Stevens scissors until the sclera is exposed. A long tenotomy hook is passed under the insertion and the upper end of the blade exposed by cutting through Tenon's capsule. Winged incisions are now made backward and outward from the upper and lower borders of the muscle, attempting to expose the muscle with as little disturbance of the circulation and lateral attachments as possible (fig. 5).

Third Stage.—Undermining the caruncle, the application of Prince's forceps, tenotomy at the insertion and excision of the muscle. The upper surface of the muscle, which should always be covered by its sheath, is now separated from the overlying tissues. This separation should be complete, especially at the internal canthus. If the muscle is stretched by the tenotomy hook and curved Stevens scissors are used, with the concavity upward, the muscle and capsule may be freed partially from the adjacent tissues by blunt dissection. One blade of Prince's forceps is passed under the muscle at right angles to the muscle, centered to grasp all the muscle and locked. In doing this the handle should always be directed

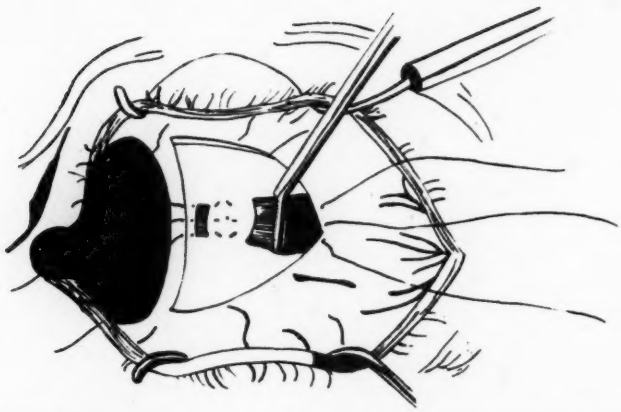

Fig. 3.—Rhomboidal suture composed of three threads, one central and two lateral. One of the lateral threads may be tightened more firmly if vertical deviation is combined with lateral deviation. (After Castresana.)

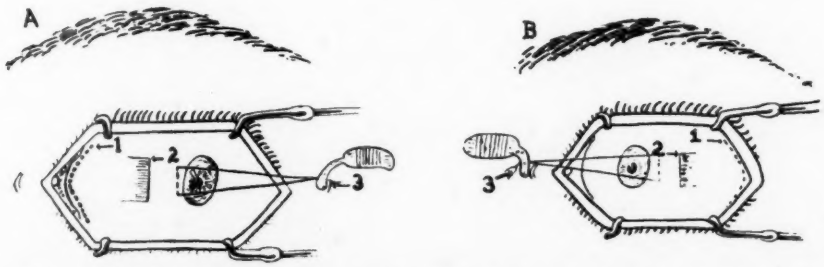

Fig. 4.—Incision at internal and external canthi and position of traction sutures (Berens). *A*, incision in the conjunctiva at the internal canthus: *1*, incision as close to the semilunar fold as possible; *2*, insertion of the internal rectus; *3*, traction suture and mosquito clamp. *B*, incision in the conjunctiva at the external canthus: *1*, incision as close to the borders of the eyelid as possible; *2*, insertion of the external rectus; *3*, traction suture and mosquito clamp.

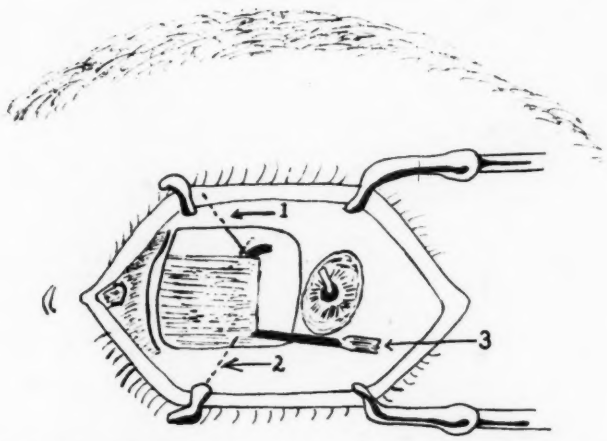

Fig. 5.—Position of lateral incisions in Tenon's capsule (Berens): *1*, upper incision; *2*, lower incision; *3*, tenotomy hook.

toward the cornea (fig. 6), and the blade should be placed 1 mm. closer to the cornea than the amount of resection desired. The measurement should be made with calipers. Tenotomy is performed with straight scissors 1 mm. from the insertion in order to leave a short stump attached to the sclera, and the excess of muscle tissue is excised within 0.5 mm. of Prince's forceps.

Fourth Stage.—Introduction of two double-armed sutures in the muscle. Two double-armed sutures of no. 3 twisted, paraffinized black silk are inserted, one at

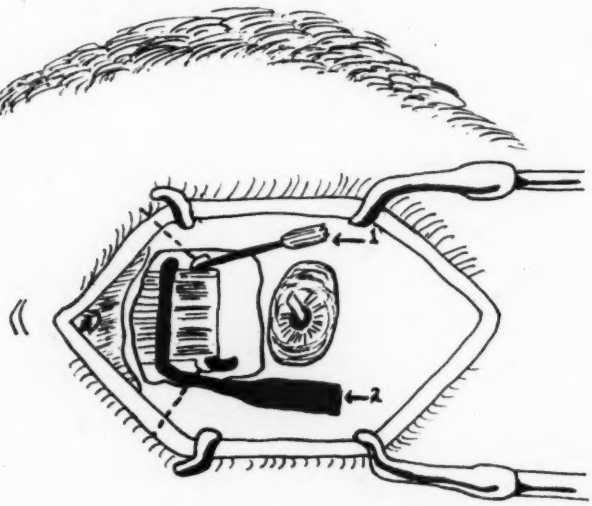

Fig. 6.—Application of Prince's forceps (Berens): *1*, tenotomy hook; *2*, Prince's forceps.

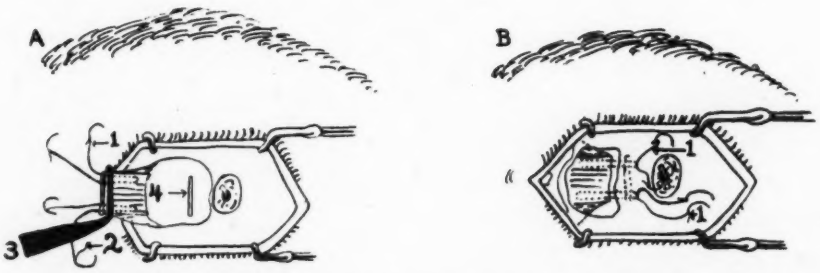

Fig. 7.—*A*, insertion of two double-armed sutures in the muscle (Berens): *1* and *2*, upper and lower sutures passing through the muscle for a distance of 5 mm. from the scleral to the outer surface; *3*, Prince's forceps; *4*, tendon stump. *B*, sutures passed through the tendon stump and conjunctiva and partially tied: *1*, upper and lower sutures.

the upper border and one at the lower border of the muscle. The needles are introduced in the scleral surface of the muscle, 5 mm. back of Prince's forceps, and passed within it to emerge on the outer surface in contact with Prince's forceps (fig. 7 *A*). The forceps are now removed, and the sutures are passed through the stump of the muscle and the conjunctiva. An attempt is made to penetrate the conjunctiva, which will eventually be directly over the stump of the muscle. Rub-

ber tissue, Wiener's gold strips and other substances have been discarded since experience has shown that they produce atrophy of the underlying conjunctiva. The suture knot will be buried deeply under the conjunctiva if the needles are passed through the conjunctiva close to the cornea. The first half of a surgeon's knot is now made, and the cut muscle is drawn into apposition with the stump (fig. 7 *B*).

Fifth Stage.—Closure of the conjunctival wound and adjustment of the muscle sutures. The conjunctival wound is now closed with a running suture of no. 1 paraffinized black silk beginning and ending in the semilunar fold (fig. 8). One should attempt to apply the suture as close to the edges of the conjunctival wound as possible, and closure should be perfect to prevent granulation and infection. The deviation is measured, and if the correction is satisfactory, the suture is immediately tied. If greater correction is desired, the sutures are tightened lightly, and the deviation is again measured. When satisfied with the correction, the surgeon's

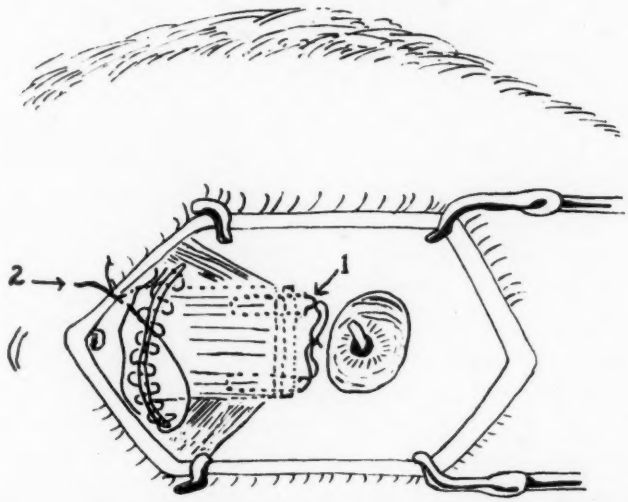

Fig. 8.—Sutures at the completion of the operation (Berens): *1*, sutures through the muscle and stump tied on the outer surface of the conjunctiva and these ends tied together; *2*, running suture closing the conjunctival wound, beginning and ending in the semilunar fold.

knot is completed, and the ends of the suture are tied together with another surgeon's knot (fig. 8).

AFTER-TREATMENT

1. A 2 per cent solution of mercurochrome-220 soluble and 1 : 5,000 oxycyanide of mercury ointment are placed in the conjunctival cul-de-sac, and a compressing dressing is applied.

2. All dressings are removed and iced boric acid compresses applied after twenty-four hours and continued every two hours for one-half hour until all reaction subsides.

3. A Ring's mask is worn with two holes centered before the eyes, partially to control their position.

4. Stereoscopic exercises are begun as soon as the patient is able to do them, and prism converging or diverging exercises are prescribed, as indicated, as soon as the deviation can be measured.

5. The solution of mercurochrome and oxycyanide of mercury ointment are used every day for one week.

6. The conjunctival stitch is removed after four days, and the deeper sutures, after seven or eight days.

COMMENT ON THE INDICATIONS FOR RESECTION

Experience seems to indicate that properly performed retroplacement operations will often render it unnecessary to perform resection, an operation in which the muscle tissue is destroyed. Advancement, in my opinion, may be entirely replaced by resection.[2a] Jameson was the first to point out to me that I would probably perform fewer resection operations as my experience with retroplacement increased. Although I did not agree with him then, now I rarely perform resection unless retroplacement combined with orthoptic training has failed to correct the deviation, or retroplacement is contraindicated. The reason for my present adherence to Jameson's original teaching is that the retroplacement operation combined with orthoptic training permits the correction of most cases of esotropia without the necessity for further operations and without unduly weakening abduction, adduction, prism convergence or the patient's ability to sustain convergence at the near point. Retroplacement is usually performed under a general anesthetic, and the results can be more accurately determined than when resection is employed; no muscle tissue is destroyed, and the action of the spasmodic muscle is weakened. My experience indicates that it is the spasm of the muscles which usually prevents patients from obtaining single binocular vision and from developing amplitude of fusion.

Exophoria and Exotropia Due Primarily to Divergence Excess[10] *or to Convergence Insufficiency.*—Retroplacement of one or both externi is performed, and orthoptic training is given before resorting to resection unless: (1) the deviation is great, (2) the deviating eye is amblyopic or (3) bilateral retroplacement of 4.5 mm. undercorrects the existing deviation. Limitation of adduction has resulted in several patients on whom resection of the internal recti had been performed.

Alternating Esotropia.—Resection of one or both externi is never resorted to unless: (1) retroplacement of the interni has failed to

10. Berens, C.; Hardy, L., and Stark, E.: Divergence Excess, Its Incidence, Its Correlation with Refraction, and the Value of Orthoptic Treatment, Tr. Am. Ophth. Soc. **27**:263, 1929.

overcome the deviation; (2) adduction of one or both eyes is deficient; (3) the deviation is of low degree, or (4) the near point of convergence is remote. In these cases, as a rule, there is bilateral overaction of the internal recti, and, unless the action of these muscles is weakened, it is usually difficult to obtain fusion.

Monocular Esotropia.—If the error is high and the deviating eye is amblyopic and if the internal rectus of this eye is spasmodic and the patient refuses to permit retroplacement [2b] of the internal rectus of the nondeviating eye, resection of the external rectus and retroplacement of the internal rectus of the deviating eye are performed.

Esophoria and Low Degrees of Esotropia.—Resection of one or both external recti or partial central tenotomy of one or both internal recti may be indicated, the decision resting on the amount of overaction of the internal recti and whether or not the near point of convergence is normal. If adduction or convergence is limited, it is preferable to perform resection.

Hyperphoria and Hypertropia.—If hyperphoria or hypertropia is associated with esophoria or esotropia, it is usually safer to perform resection than retroplacement or recession because of the difficulty of obtaining fusion and the danger of secondary deviation.

SUMMARY

Resection by the Reese method has been attended by complications that have been eliminated by the technic described here. The principal features of this technic are:

1. A curved conjunctival incision, with the concavity toward the cornea, far from the stump of the muscle, which reduces the visible postoperative scarring and lessens the tendency to granulation and infection.

2. Winged incisions from the insertion of the tendon and no disturbance of the capsule of the muscle, which should decrease the tendency of the muscle to become atrophic.

3. Two double-armed sutures so placed in the muscle that their action may be increased after the conjunctival wound is closed, and their bite so secure that the dressings may be removed the day following the operation.

The indications for resection have so diminished since retroplacement has been used that I now perform many more retroplacement operations than resection operations.

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ABSTRACT OF DISCUSSION

DR. LUTHER C. PETER, Philadelphia: Like the cataract operation, the number of procedures proposed for the correction of squint is evidence of the fact that operators are impressed with the need for greater refinement and accuracy in its operative treatment. In the interesting presentation of Dr. Berens, many phases are opened for discussion. I can agree entirely with many of the conclusions drawn. Others are not in perfect accord with my experience, but differences in opinion are largely the result of varied experiences.

In regard to the relative value of resection, advancements and recessions, each has its special merits and its indications. In my experience, recessions or retroplacements should be regarded largely as supplementary to advancements and resections.

Reasons for this belief are to be found in the relaxed, thinned out and flaccid condition of the external rectus and capsule. The muscle is stretched to the extent of the deviation. To restore it to normal function by shortening or by giving to it, in addition, better mechanical purchase on the globe, is, in my judgment, a better surgical procedure than to break the pull of the internus, which, after all, is in a normal state, but contracted, because it is feebly opposed. A recession or even a questionable tenotomy of the internus will net one a maximum correction of 12 degrees. Mellor says: "It is commonly believed that tenotomy of the internal rectus corrects to the extent of fifteen degrees, but often there is produced decidedly less correction, and sometimes even much less." In my experience, a maximum gain of 12 degrees can be obtained if the tenotomy is correctly performed. A recession suture will not accomplish more within the safe limits of retroplacement. It is only when combined with resection or advancement that recession can really accomplish maximum results. Because it can be so carefully regulated, it offers an ideal supplementary procedure under certain conditions, after the external rectus has been properly shortened.

In comparing the value of resection and advancement, there should be uniformity of opinion. Each has its indications, and these indications are determined by the degree of squint to be corrected. Resection of the external rectus should not go beyond the length of the tendon, which is 8.8 mm. If a greater section of the tendon is to be excised, a properly performed advancement of the Worth type is of more value, because the entire tendon need not be sacrificed, and a gain of at least 5 degrees, or even more, can be obtained. It is manifestly inadvisable, therefore, in my judgment, to feel that a resection in itself can replace an advancement in certain cases, in squint, for example, of 15 degrees or more. I have repeatedly placed myself on record, however, as being opposed to attempting to overcome too wide a degree of squint by shortening of the external rectus alone, without a supplementary procedure such as a recession of the internal rectus on the same eye or an additional resection or advancement on the fellow eye.

There are specific indications for each of the three operations, and each should be selected with reference to the needs in an individual case. In general, however, recession should be held in reserve as a supplementary procedure. If the internus is in a state of contracture, in squint of long standing and of wide degree or in paralysis of the externus, the internus may first be set back to a safe point on the sclera, and shortening of the externus becomes the supplementary operation.

In regard to the various types of resections, I can entirely agree with Dr. Berens that the Reese technic is faulty in several details, and, after all, refinement of detail is an important factor. In the Reese resection and in most resection operations practiced, there is too much disturbance of the capsule and the muscle sheath. Too much scar tissue is created. In the second place, the muscle sheath under the

muscle should not be disturbed or injured, but should be preserved intact as a lining for the muscle to prevent adhesions to the sclera. The third objection is the introduction of the sutures from the scleral surface instead of from the conjunctival surface. This important phase of the operation is rarely considered. It is responsible for imperfect coaptation of the conjunctiva and the occasional resulting exuberant tissues.

Among the most widely practiced resection operations, Dr. Berens failed to mention the Worth method. This probably was omitted because it is generally known as an advancement procedure. However, it is applicable to resection; it is efficient in its correcting power and is most satisfactory cosmetically. From a surgical standpoint, it causes a minimum of disturbance of the muscle, capsule and conjunctiva, insures fascial lining for the under surface of the muscle, firmly coapts the two cut ends of the tendon and the conjunctival surfaces and advances the capsule, which is an important feature in the end-results.

In adolescents and in adults the operation proposed should be satisfactory. I believe, however, that the sutures should be introduced from the conjunctival surface rather than from within out. In young children, as suggested by Dr. Berens, ten day chromic catgut will obviate the necessity for the removal of sutures. This is an advantage. The running conjunctival suture offers no difficulty in removal.

The two outstanding phases of the procedure practiced by Dr. Berens are the conjunctival incision and closure of the wound by a running suture, which is not tied. This treatment of the conjunctiva is applicable to many of the resection operations practiced. They are measures which yield ideal local cosmetic results. A third commendable feature is the effort to preserve the muscle sheath and the capsule of Tenon.

It is interesting to note that tucking was not included in the operations under consideration. Dr. Berens has endeavored to correct the errors in technic of the Reese resection, and naturally tucking was not discussed. It, too, has specific indications for use, but from a surgical standpoint it does not possess the refinements in local cosmetic appearance that one can obtain from a correctly performed resection or advancement.

In regard to the specific indications for each type of operation in cases of phoria, one should determine, in esophoria, whether the case is one of excessive convergence or of subnormal divergence; in exophoria, one should determine whether the divergence is abnormally strong or the convergence is too weak. An excessive convergence in the first type of case and an abnormally great divergence in the second type call for a recession type of operation to restore a normal balance. If divergence in esophoria and convergence in exophoria are subnormal, a shortening operation on the weak muscle will yield the best results.

Dr. W. T. Davis, Washington, D. C.: It would seem well to emphasize several of the excellent conclusions reached by Dr. Berens in his paper.

Incisions made during resection operations take longer to heal and may cause postoperative disfigurement. The effect cannot be so accurately gaged as with the recession operation. Advancement leaves a mass of tissue, which, being composed of muscle, may remain red and disfiguring.

In cases of esotrophia, double recession is preferable to resection or advancement; from 25 to 30 degrees of correction may be obtained in this manner. In cases of exotropia, recession has not been found of much value except in conjunction with resection, advancement or both.

Recession as done by Jameson is masterful in its simplicity. It is the ideal operation for children, particularly when done with avertin as the basal anesthetic. There is no tension on the sutures, thereby conforming to a cardinal surgical prin-

ciple. Since gut is used, there are no sutures to be removed, thus relieving both patient and surgeon from a most distressing experience. Healing is prompt and without scarring.

Dr. Berens' operation of resection fulfills some of the important qualifications of the Jameson operation, in that it does not disturb the nerve and blood supply of the muscle or its fascial covering, and also in the use of the semilunar fold incision and dissection as originated by Jameson.

I should like to ask Dr. Berens whether he has at any time had any unpleasant results from damming of the secretions. Since the conjunctival incision is distant from the point of union of the muscle end with the stump, one might fear lack of drainage.

I congratulate Dr. Berens on his paper and on his operation. The adaptation of the semilunar fold and the other mentioned attributes of the Jameson recession to his resection certainly gives it many advantages.

Dr. Walter B. Lancaster, Boston: I endorse Dr. Berens' improvement on the Reese operation, but I wish he had gone a bit further. I shall attempt to show on the blackboard a still further improvement.

It concerns the method of attaching the resected muscle to the eyeball, that is, to the stump of the tendon. Reese and Berens follow the plan of Noyes (1874). The suture is first passed through the muscle, both needles from the scleral side outward or forward. The muscle is held in Prince's forceps while this is done. Next the needles are passed through the stump of the tendon, in the same direction, namely, from the scleral or posterior surface forward. When the suture is pulled up and tied, Prince's forceps must first be removed. There is, then, nothing to hold the muscle forward in its new position while the stitch is being tied. The operator must rely wholly on the part of the stitch through the muscle to pull the muscle forward into its new position under the tendon stump. Once it is securely tied, there is no further danger of slipping, because it is a mattress suture, clamping the two surfaces firmly together.

My contention is that it is better to begin by passing the suture first through the stump of the tendon, both needles from the scleral or posterior surface forward. Then both needles are passed through the muscle behind Prince's forceps. When the surgeon ties the sutures, the assistant holds the muscle by means of Prince's forceps in one hand, while the eyeball is rotated toward the muscle by fixation forceps, in the other hand, applied over the antagonist muscle on the opposite side of the cornea. The muscle is held over its new attachment by forceps, so that the stitch does not have to pull the muscle forward to its new attachment. Thus the surgeon need have no fear that the stitch may slip during the critical moments while it is being tied. After it is tied, Prince's forceps are removed, and the end of the muscle may be cut off or left to shrink and adhere to the sclera.

The stitch may be passed in this manner, whether it is to be a buried suture or whether the needles are finally passed through the conjunctiva and tied outside the conjunctiva, provided the incision in the conjunctiva is chosen with this in view and provision is made for the forceps to hold the muscle.

Dr. Otis Wolfe, Marshalltown, Iowa: I wish to cite the advantages of the Briggs silver ring for young children. If the muscles were always well developed, there would be no occasion for using a technic of this kind; but with small, undeveloped muscles I believe in the value of tucking rather than advancement in children. The Briggs ring enables one to include the capsule and the conjunctiva and will hold. If the dressings are removed the next morning, the child seldom has to be kept in the hospital longer than one day. In children it is well to uncover the

eye in a few hours. This has a distinct advantage, in that fusion exercises can be begun the next day.

During eight years I have never had an infection and I have never had one slip. When the child is allowed to go home, you can be certain that when it returns to your office the eye will be in the same position as when the child left the hospital. I think that the method also has the advantage of allowing one to operate on a child at any age. I have had patients from 2 years up. The Briggs ring enables the child to begin exercises early.

DR. CONRAD BERENS: Dr. Peter prefers advancement of the external rectus in many cases of convergent strabismus due to excess of convergence. My experience has been that, unless the spasmodic medial recti are weakened, fusion is seldom obtained. Unless there are definite contraindications, retroplacement is performed, and this procedure has proved satisfactory in many young children who have been operated on under general anesthesia.

To introduce the sutures from the conjunctival surface has proved technically more difficult than to introduce them from the scleral surface. No complications have arisen from this method of introducing the sutures. I am indebted to Dr. Peter for stressing the necessity of studying patients from the standpoint of anomalies of divergence and convergence, and I follow this procedure in practice according to Duane's teaching. However, the terminology is confusing to certain ophthalmologists.

As I have had no experience with the method suggested by Dr. Wolfe, I am unable to discuss the question he raised.

My experience is apparently contrary to that of Dr. Davis in exophoria and exotropia due to excess of divergence. Retroplacement combined with prism converging exercises has produced satisfactory results in the majority of cases.

There has been no difficulty due to retained secretion because of the method of suturing advocated.

Dr. Lancaster has raised several important questions. In answer, I have not found it necessary to suture the muscle over the stump, and possibly the sutures have held because the capsule is not disturbed.

The suggested incision gives free access to the muscle, and the resulting scar is so situated that the cosmetic result is good. No difficulty has been experienced owing to the fact that the proposed incision cuts the vascular supply to the conjunctival flap, and because the incision is not placed over the muscle, stump granulation and infection are less likely to occur.

ANGIOID STREAKS OF THE RETINA AND PSEUDOXANTHOMA ELASTICUM

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The term "angioid streaks of the retina" was first employed by Plange in 1891 to describe certain changes in the fundus characterized by reddish-brown striae, radiating from the border of the disk and often extending beyond the equator. Like changes had been described by Doyne in 1889 without any attempt at classification. Since that time there have been forty reports in the literature, all of which had similar clinical characteristics.

Visual disturbances may or may not occur, and the disease, therefore, is often encountered in the routine examination of the fundus. The process, however, apparently is acute, being characterized by the formation of hemorrhages, exudates and striae. There is usually a reddish-brown band, varying in width around the optic nerve, which may or may not be complete. Extending from this band there are one or more irregular lines that assume the course and distribution of blood vessels. These lines appear to communicate near the border of the disk, and toward the periphery they often branch. All authors agree that these striae lie beneath the retinal blood vessels, which in the majority of cases have been reported normal. Also one of the most frequent findings has been a central choroiditis. It seems quite evident from a study of the reported cases that the extent of intra-ocular pathologic changes, such as chorioretinitis, central choroiditis and hemorrhage, is dependent on the number of streaks present. The hemorrhages and exudates clear up after a few months, leaving the choroidal changes, but the streaks may remain apparently unchanged for years. However, along some of the streaks there may eventually occur a complete atrophy of the choroid.

The histopathology of angioid streaks remains unknown, as no authentic case has been studied. Lister reported a case that was studied microscopically, but which was not evidenced with an ophthalmoscope. His case showed new-formed blood vessels enveloped in pigment in the outer layer of the retina. Magitot reported the microscopic observations in a case as regressive changes in old hemorrhages, but other observers

Read before the Section on Ophthalmology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 13, 1932.

did not believe his case one of angioid streaks. Verhoeff's report of pigmented streaks does not fall in this classification.

There are many explanations for the formation of these streaks. Plange, de Schweinitz, Pagenstecher, Holden and others explained the streaks as due to hemorrhages. Coppez (1922), Axenfeld, Guist and others believed that the folding of the pigment layer of the retinas produced by some exudative process was the explanation for the streaks. Calhoun suggested as the cause some disease of the vascular system that might be familial in origin. Kofler explained the streaks as tears in the glass membrane as a result of a degenerative process. None of the foregoing theories seems to be quite plausible, because the pathologic lesions described in angioid streaks have all maintained a singularly characteristic position in the fundus. Treacher Collins' explanation is more reasonable, but it is not true pathologically. His statement, "that the uniformity of arrangement of the streaks in the different cases at once suggests that there must be some anatomical factor upon which their distribution depends," certainly is reasonable, but to explain this as being due to a peripheral choroidal hemorrhage with the collection of blood pigment along the perivascular lymph spaces of the posterior short ciliary arteries is not true pathologically. In the majority of cases reported the patients have been fairly healthy and past middle life, so that the occurrence of retinal or choroidal hemorrhages without any positive common findings is not consistent. Neither does it seem consistent to consider it as a vascular disease, since the retinal vascular system as a whole is fairly normal.

Grondblad and Marchesani and Wirz have recently reported the association of angioid streaks of the retina with a rare disease of the skin known as "pseudoxanthoma elasticum." Marchesani and Wirz explained the occurrence of angioid streaks in the light of the known pathologic changes of pseudoxanthoma elasticum, believing that the two conditions are clinical manifestations of the same pathologic process. These authors proposed the theory that the formation of the striae is due to the degeneration of the lamina elastica of the choroid. However, the present knowledge of the pathology of the lamina elastica of the choroid and pseudoxanthoma elasticum of the skin does not support this theory.

The term "pseudoxanthoma elasticum" (elastorrhexis of the skin) refers to a rarely encountered disease of the skin characterized by the occurrence, usually early in life, of buff-colored, faint yellow or orange, linear or punctate discolorations, occurring in the skin of the neck, axillary folds, cubital fossae, popliteal spaces and sometimes the abdomen and chest. There is always a loss of elasticity in the affected areas, and often there is some atrophy and even scarring. On close inspection the diseased areas have an appearance of small, light orange-colored

tumefactions under the skin. The disease produces no subjective symptoms and is more often discovered by women, purely as a consmetic defect. While the disease occurs in members of the same immediate family, there is no definite evidence to support any statement as to its hereditary nature. The disease may be slowly progressive, but no case has been observed over a long enough period to be sure of this observation. Whether pseudoxanthoma elasticum is really a separate disease has not been definitely proved to my satisfaction. It is probably a form of degeneration of the elastic tissue of the entire body, for some reason more marked in isolated locations than in others, for the same cutaneous changes with only minor variations have been found in the skin of patients with pseudoxanthoma elasticum and senile elastosis and also in skin supposedly normal from a patient 85 years of age. There was nothing in any of the specimens examined to indicate that the disease is a neoplastic process. Rather, some of the earlier changes in the skin might suggest a low grade infectious process, for in these one finds more lymphoid infiltration and endothelial proliferation especially about some of the vessels with an appearance suggestive of a tuberculous process. No giant cells were found in any of the sections of the various cases, and there have been no degenerative changes except that affecting the elastic fibers. Sections have been especially studied for the fatty changes described by Weidman, but no such changes have been noted.

As the histopathology of all the cases examined has been essentially the same, I shall give in detail the microscopic description of only one. Sections were made lengthwise of the skin to show the entire thickness, and were stained with hematoxylin and eosin, Verhoeff's elastic tissue stain and frozen sections with sudan III. The surface is mostly flattened, although some portions show a wavy outline. There is a thinning of the epithelial layer with shortening and in some places complete absence of the pegs. There is slight brownish pigmentation of the basal cells, no pigment being found outside this layer of epithelium. There is no marked hornification or scaling on the surface. The superficial portion of the derma is seen as a thin layer of acellular connective tissue, which is replaced by masses of elastic fibers, some of which are represented by masses of granular amorphous material. The more marked changes are seen deeper, where large masses of this degenerated elastic tissue are found lying between bulky strands of connective tissue. Taken all together, there seems to be an increase in amount as well as a degeneration of elastic tissue. There are no vascular changes of a marked degree. There seems to be a slight tendency for granules of degenerated elastic tissue to collect about some of the vessels, with perhaps a little thickening of the wall. The glands and hair follicles show no deviation from the normal.

From the histologic standpoint the condition must be assumed to be a proliferation and degeneration of the elastic tissue of the skin, which changes are closely related to the normal aging process found in senile skin.

Before discovery of the articles of Grondblad and Marchesani and Wirz, three of the following cases were presented before the Atlanta Eye, Ear, Nose and Throat Society to illustrate the unusual occurrence of the two diseases in the same person.

Fig. 1 (case 1).—Angioid streaks of the retina.

REPORT OF CASES

CASE 1.—Mrs. J. W., aged 46, consulted me in June, 1923, complaining of pain in the eyes following close work. Examination revealed a small compound myopic astigmatic error and presbyopia. This combination gave her normal vision. Examination of the fundus showed it to be normal. She consulted me again in June, 1925, complaining of poor sight for the past month. Vision in the right eye was 20/40; that in the left, 20/70. Examination of the right fundus showed: media clear; nerve head oval; rings present; cup shallow; arterial reflex stripe conspicuous; slight arteriovenous compression. The most conspicuous lesion was a reddish-brown one partly around the nerve head under the retinal blood vessels and extending out from this four small streaks resembling blood vessels. Along a

streak opposite 3 o'clock was an area of choroidal atrophy with a hemorrhage. The macula looked granular. The left fundus had the same appearance. Complete physical and laboratory examinations gave negative results.

In June, 1931, vision in the right eye was 20/70; that in the left, 20/40. Some of the streaks had disappeared, and along these areas there was marked choroidal atrophy. The appearance of the nerve head and retinal arteries and veins was normal. Examination of the skin by Dr. Jack Jones and Dr. Herbert Alden at this time showed the following: The skin of the neck, anterior axillary folds, cubital fossae, lower part of the abdomen and popliteal spaces was relaxed and

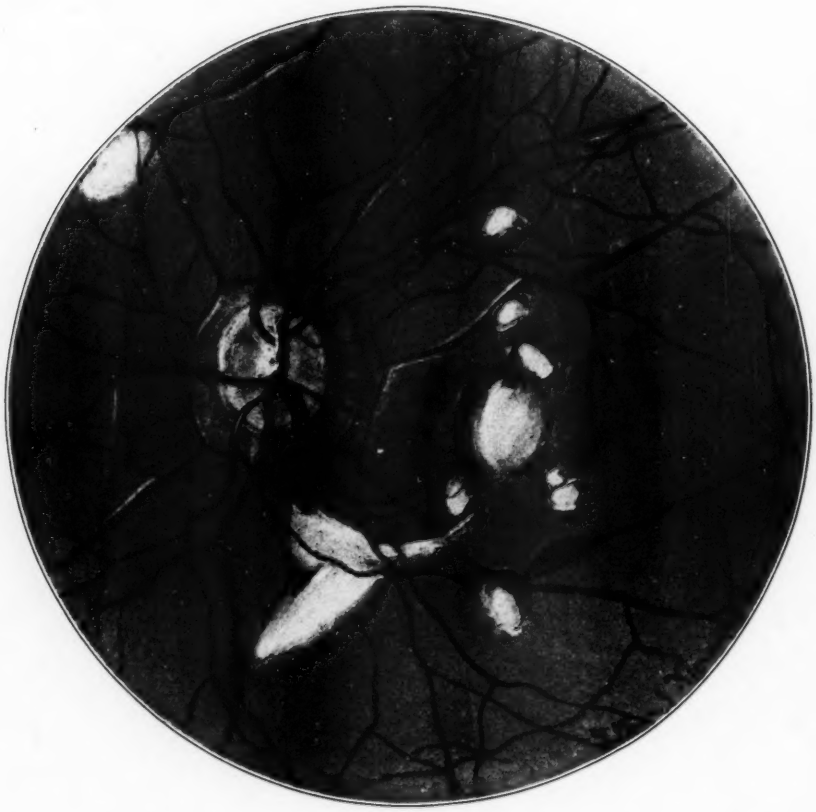

Fig. 2 (case 2).—Angioid streaks of the retina.

inelastic. There was a rather marked linear "scarring" on the neck, associated with a finely reticulated atrophy. In the axillae, cubital fossae and popliteal spaces was a light yellow or buff-colored discoloration that appeared as faint scarring, but which on stretching and closer examination was made up of a number of orange-colored subcutaneous tumefactions within the skin. On palpation, these areas had a smooth velvety feel. The diagnosis was pseudoxanthoma elasticum.

The following case was reported by Dr. F. P. Calhoun:

Case 2.—W. C. H., aged 35, a physician, noted dimness of vision in July, 1925. He was first seen in March, 1926. Vision in the right eye was 10/100; that

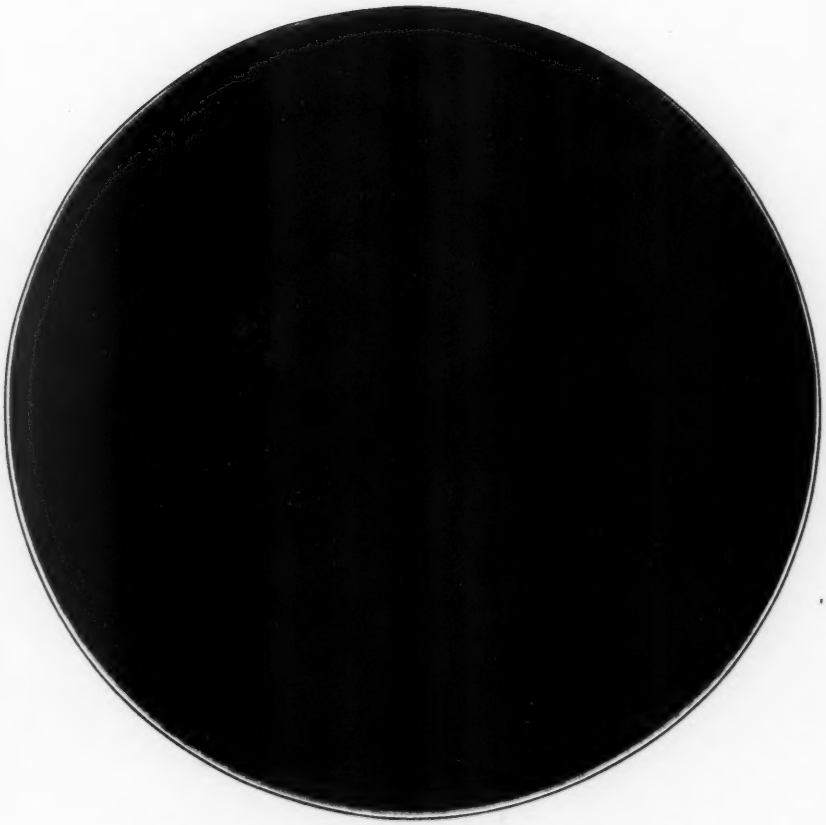

Fig. 3 (case 3).—Angioid streaks of the retina.

in the left eye, 20/50. Ophthalmoscopic examination of the right eye showed clear media. The disk was round and had a yellowish tinge. The cup was shallow, and from it emerged normal vessels, passing evenly across the margins of the disk, which were slightly pigmented and hazy. The retinal vessels were normal in size and caliber throughout their course. A short distance from the margins of the disk was an incomplete, irregular, brownish ring, from which extended various anastomosing branches. These lines varied in size and color. Toward the equator of the globe, where some of them terminated, they abruptly lost their net-like arrangement and gradually took on the course of retinal vessels. Some of the streaks appeared to be at a deeper level than others, and where two lines crossed the color was darker. To the nasal side of the disk a broad, fairly straight, pigmented streak, being an extension of a curved one, ran obliquely upward and inward, and terminated in a small punched out area of choroidal atrophy. A dense white line followed its course on the outer side. Two disk diameters above the disk was a small atrophic area in the choroid, and in the macular region a similar but larger area with its borders heaped with pigment. Over these pathologic lines and areas coursed the retinal vessels in a normal manner, without visible communication.

The left fundus was similar, but its changes were more extensive, in spite of better vision. The brownish lines around the disk were more broad and irregular in size and had a more netlike arrangement. Whitish streaks bordered many of the brownish lines, when they were straight and ran any distance. Above and below the disk were areas of dense scarring in the choroid, besides several smaller ones situated within, above and below the macular region. Many of these brownish lines seemed to communicate with the patches of choroidal atrophy. On each side of and below the macular pathologic changes were long extravasations of blood which appeared to be in the outer retinal layers, for the retinal vessels passed over them. As in the right eye, the retinal circulation was normal throughout, and the vessels passed over the choroidal areas and brown lines without communication. The diagnosis was angioid streaks of the retina.

Complete physical and laboratory examinations gave negative results.

In June, 1931, the patient stated that his vision had been better, and that he had been able to resume the practice of medicine. He said that one sister and aunt had a similar ocular condition and pseudoxanthoma elasticum of the skin. The picture of the fundus at this time showed more choroidal atrophy in the region of some of the streaks. Many streaks were still visible and had the same appearance as in 1925. The retinal vessels were normal. Examination of the skin by Dr. Jones and Dr. Alden showed the following: The skin of the neck was rough and inelastic. On stretching the skin, the apparent roughness disappeared and one could see a number of small, linear, buff-colored areas which appeared deep in the cutis. The skin of the anterior axillary folds, cubital fossae and popliteal spaces was covered with a finely reticulated mottling that took on a linear aspect on stretching. These areas had an appearance of very fine scarring. The diagnosis was pseudoxanthoma elasticum.

Case 3.—E. F., a white man, aged 44, an American, a minister, consulted me in October, 1930, complaining of poor vision for the past five months. One sister and maternal aunt had complained of poor vision. As a young man he had malaria fever and pneumonia and recently had undergone tonsillectomy. His health for the past several years had been good. External examination gave negative results. The pupils and muscle excursion were normal. Vision in the right eye was 20/30; that in the left, 20/30-2. Examination of the fundus of the

right eye showed: media clear; disk oval vertically; PD + LC; rings +. Immediately surrounding the disk was a narrow ring of hemorrhage; radiating from the disk was a series of long, irregular, dark red streaks extending well out in the periphery of the fundus and lying beneath the retinal vessels and in places were crossed by them. They were most marked temporally above and below. One small short streak extending from the disk about 7 o'clock and about 2 disk diameters in length bifurcated, and there were whitish streaks on the edge. In the

Fig. 4 (case 3).—Low power view of the skin, showing the pathologic picture in a case of pseudoxanthoma elasticum.

periphery were innumerable small round hemorrhages apparently lying in the choroid. Temporally and below the macula the choroid was beginning to undergo honeycomb degeneration; the macula appeared normal. The retinal vessels also appeared normal.

Examination of the left eye showed: media clear; disk round, PD+ LC+. This eye presented an appearance similar to that of the right. The ring of hemorrhage around the disk was not quite so broad. Between the disk and the macula, underlying the retina, was a whitish area somewhat triangular in shape; the margins were sharp; the upper point of the triangle was bifurcated; radiating streaks were noted

in the right eye; slightly more pronounced and deep-lying choroidal hemorrhages were numerous. No lesions were seen in the macula. The diagnosis was angioid streaks of the retinas of both eyes.

In November, 1930, the patient saw Dr. de Schweinitz in consultation. His diagnosis confirmed my opinion. The man had a complete medical examination while in Philadelphia and was reported entirely normal except for a lesion of the skin resembling pseudoxanthoma elasticum. After his return from Philadelphia, Dr.

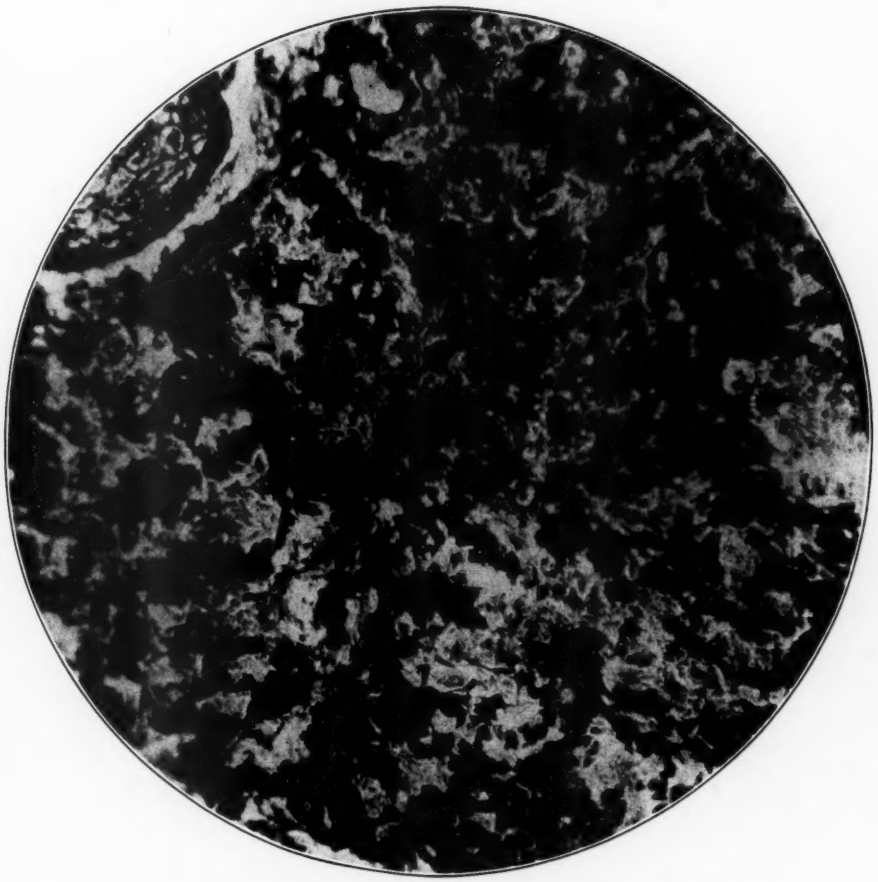

Fig. 5 (case 3).—High power view of the skin, showing the pathologic picture in a case of pseudoxanthoma elasticum.

Jones and Dr. Alden examined the cutaneous lesions and confirmed the diagnosis of pseudoxanthoma elasticum. This report was as follows: The skin of the neck had a definite loss of elasticity and appeared roughened. There was a buff-colored, linear discoloration that was made more apparent on stretching. Some of the areas had the appearance of faint scars. The skin of the anterior axillae, cubital fossae, lower part of the abdomen and popliteal spaces presented the same buff or light yellow-colored mottling as the neck. In these areas there was also a loss of elasticity.

In March, 1931, vision was better and examination of the fundus showed that the hemorrhages had disappeared, leaving the streaks the same as at the first examination.

CASE 4.—Mrs. E. C., aged 46, a sister of the patient in case 3, was first seen in January, 1931. Her general health had always been good. Six weeks prior

Fig. 6 (case 3).—Photograph showing lesions of the skin, pseudoxanthoma elasticum.

to examination she began to notice a blur before the left eye, which she thought came on suddenly. There had been no improvement in sight since that time. There had been no disturbance of sight in the right eye. External examination gave negative results. The pupils were normal; muscle excursion was normal, and the tension was normal. Vision in the right eye was 20/20; that in the left, 20/200. Examination of the fundus of the right eye showed: media clear; nerve

head oval; long axis 90; rings present. There was a large cilioretinal artery at the border opposite 11 o'clock which supplied the entire superior nasal field. It was larger than the superior nasal artery, which sprang from the central vessel. The arteries and veins were normal in caliber. Near the border of the disk from 11 o'clock extending around to 5 o'clock under the retina and retinal blood vessels, there was a reddish area that looked like a blood sinus. It was irregular in outline, and extending from it opposite 12 o'clock under the retina directly upward and slightly irregular in course was a dark reddish streak that had the appearance of

Fig. 7 (case 4).—Angioid streaks of the retina.

a vein; just nasally from there was a much larger streak that extended up and in and then out into the extreme periphery. In the periphery along this streak was some black pigment. Opposite 3 o'clock was another small offshoot that extended directly out nasally; then there was a fresh one from that, which extended about one-half disk diameter from the border of the disk down and parallel to the border of the disk to the point of about 5 o'clock, from which point it extended down and out into the periphery. This looked like a blood sinus; the borders were irregular, and it appeared to be deep in the choroid. No other arteries were seen. The retina appeared normal; the macular region showed no lesion.

In the left eye the same condition was found, except the blood spaces were more conspicuous, and in the macular region there was a large horse-shoe hemor-

rhage surrounding the macula, which apparently lay in the retina. The macula was granular. At the border of the disk opposite 3 o'clock there was a blood sinus that continued out toward the macula and then swooped down and extended to the extreme periphery. Along this sinus there was a marked amount of choroidal pigment.

The diagnosis was angioid streaks of the retina.

The patient was seen by Dr. Jones and Dr. Alden, who made a diagnosis of pseudoxanthoma elasticum. Their report was as follows: The skin of the anterior

Fig. 8 (case 5).—Angioid streaks of the retina.

axillary folds of the neck and cubital fossae presented a fine, linear, pale, yellow marking. On stretching of the skin, the lesions appeared as within it, as small tumefactions. There was a slight loss of elasticity in these areas.

The patient lived in Florida and could not remain for further study. Her physician reported negative results of physical and serologic examinations.

Case 5.—Mrs. J. J. C., aged 45, was first seen in June, 1931. Her general health had been fairly good except during her three pregnancies; she was very sick during the last one, in 1913; she had had convulsions. There was no ocular trouble in the family. The eyes ached, and she had pain and headaches following close work. External examination gave negative results. Her refractive error was one of compound hyperopic astigmatism, which gave her normal vision. Exam-

ination of the fundus of the right eye showed: media clear; nerve head oval; long axis 90; scleral ring present; cup shallow; lamina cribrosa absent. There was some retraction of the choroid, with choroidal atrophy opposite the nerve head above and some all the way around the nerve head. The choroidal vessels around the nerve head could be seen clearly. There were a few areas of brownish pigment around the nerve head. At the border of the disk opposite 12 o'clock there was a brownish streak that extended up under the retina, had the appearance of a blood vessel, extended up for about a disk diameter in length and disappeared.

Fig. 9 (case 6).—Angioid streaks in the retina.

The choroid in this area was distinctly granular. There was a brownish line around the nerve head, extending from 12 o'clock around to 7. This line was in the area in which the choroidal atrophy was most marked. It had the same appearance as the streak, which extended upward. The arterial reflex stripe was present; the arteries were normal in caliber; the veins were normal; no lesion was seen in the retina. The retinal arteries and veins were normal.

Examination of the fundus of the left eye showed: media clear; nerve head round; scleral ring present; cup shallow; lamina cribrosa absent; at the border of the disk extending from 11 o'clock to 2 and up for a disk diameter, an area of choroidal atrophy through which could be seen choroidal vessels. Through this area and extending from 12 o'clock there was an irregular, brownish line which

at the base was slightly broader than the central vein and extended directly up through the middle of this area and for a distance of about one-third the length of the lesion. Around this lesion there was a considerable amount of reddish-brown pigment, which appeared to be in the choroid. Around the nerve head was an irregular area of choroidal atrophy; choroidal vessels could be plainly seen; no further streaks could be seen. The macular region was extremely granular; the arteries were normal in caliber; the reflex stripe was normal; there was no arterial venous compression. The diagnosis was angioid streaks of the retina.

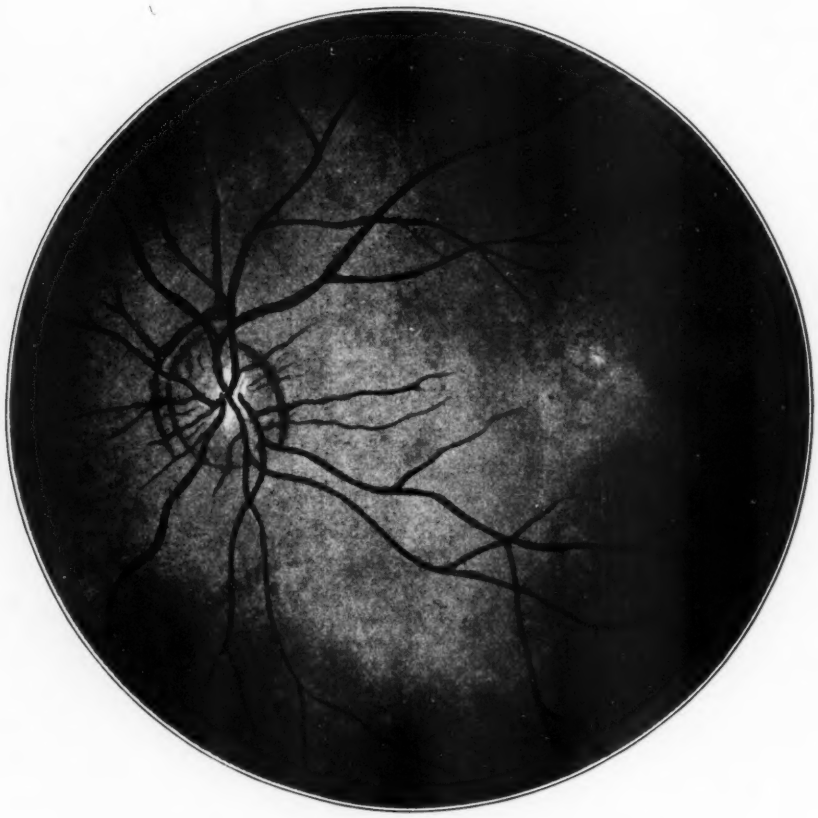

Fig. 10 (case 7).—Angioid streaks of the retina.

Medical examination by Dr. G. Mizell gave essentially negative results. Examination of skin by Dr. Jones and Dr. Alden showed senile elastosis.

Case 6.—Dr. J. S., aged 47, was seen on Aug. 5, 1931, when a diagnosis of angioid streaks of the retinas of both eyes was made. There was no history of ocular diseases in the family. His general health had not been good for the last eight months; he had had diabetes mellitus, though he remained sugar-free. Recently his near vision had become very poor. External examination gave negative results. Vision in both eyes was 20/30. A small myopic correction gave normal vision, and +225 added, normal near vision. Examination of the fundus of the right eye showed: media clear; nerve head round; rings present; cup shallow;

lamina cribrosa absent; arteries and veins normal in appearance; reflex stripe present; around the border of the disk in the choroid, an irregular, reddish-brown area extending almost all around the nerve head. Opposite 12 o'clock there was a reddish-brown line that extended up for about a disk diameter and had the appearance of blood vessels; nasally, there were two lines that extended up for a short distance, and around both of these lines was fresh blood. Otherwise, the retina showed no gross lesion.

Examination of the fundus of the left eye showed: nerve head normal; arteries and veins good; opposite the disk border at 10 o'clock, a reddish-brown area that extended up somewhat in the course of the superior nasal artery, but disappeared at about the equatorial region; reddish-brown streaks with irregular borders temporally surrounding the disk; another reddish-brown area in the choroid, and radiating off from this, streaks of the same character. The diagnosis was angioid streaks of the retina.

Complete physical and serologic examinations by Dr. Bunce gave negative results, except for diabetes mellitus, which was under control by a diet of carbohydrates, 150 Gm.; protein, 80 Gm., and fat, 150 Gm.

On Jan. 25, 1932, the patient showed no hemorrhages. The streaks remained the same. The report of the examination of the skin by Dr. Jones and Dr. Alden was as follows: On the left side of the chest just above the nipple there was irregularly shaped, light yellow mottling about the size of a half dollar. On stretching the skin in this area the lesions became more prominent, having the appearance of being made up of a number of very fine, light orange-colored, subcutaneous tumors that were visible through the cutis. No other cutaneous lesions were found. Figures 7 and 8 show the pathologic picture of pseudoxanthoma elasticum in this case.

Case 7.—H. E. W., a white man, aged 71, had always been in good health. The family history was negative for ocular disease. Vision had been poor in the right eye for a year, and in the left eye had recently been getting dim. Vision in the right eye was limited to the perception of objects; that in the left eye, 20/200. The right eye was not improved. Vision in the left improved to 20/30 with $+20 = +50$ axis 180. External examination of the right eye showed a fairly mature senile cataract. There were no fundus details. Examination of the left eye showed: a few lenticular opacities; nerve head oval; axis, 90; rings present; cup shallow; retinal arteries small; some increase in arterioreflex stripe; veins normal; around the nerve head from 9 to 2 o'clock, an irregular, reddish-brown band; at 9 o'clock a streak of the same color, which extended out for a short distance under the retina, and the same type of streak opposite 1 o'clock, which extended to the equatorial region. The diagnosis was angioid streaks of the retina.

Examination of the skin by Dr. Jones and Dr. Alden showed the following: The skin of the body generally was dry and inelastic. On either side of the neck the skin was dark brown and much roughened. On stretching the skin and close examination, very small, light yellow tumors placed in the lines of cleavage of the skin could be seen through the translucent cutis. These lines of small subcutaneous tumors were separated by lines of fine telangiectasia. The appearance of the skin corresponded to the condition described by Weidman as senile elastosis.

COMMENT

The uniformity of arrangement of the angioid streaks in all the cases reported makes it imperative that the disease be explained on an anatomic basis.

Short posterior ciliary veins exist, but normally do not pass through the sclera with the arteries. Kuhnt and others have reported such vascular anomalies. A vascular anomaly of similar character, namely, posterior vortex veins, is rare, as stated by Salzman. However, experience has shown that veins of the posterior vortex are often observed objectively in cases of high myopia and in emmetropic eyes with little retinal pigment. Coppez in 1908 reported a case of abnormal peripapillary vascular ring which was undoubtedly one of short posterior ciliary veins. Later in 1923 he reported the same case as one in which angioid streaks of the retina had developed. The cases herein reported bear out these observations, in that there is a distinct uniformity of arrangement of the streaks in all cases. Three of the cases showed an evident vascular anomaly. Five of the patients had pseudoxanthoma elasticum of the skin and one had dermatologic evidence of senile elastosis.

Therefore, I wish to present a new theory for the causation of angioid streaks of the retina, as follows: There exist in these patients short posterior ciliary veins corresponding in their course and arrangement to the short posterior ciliary arteries, and the formation of angioid streaks is the result of a thrombosis of these veins. The thrombosis is purely mechanical, being brought about either by the increase in fibrous tissue of the sclera as the result of age, or by the degeneration of the elastic tissue of the sclera in persons who have pseudoxanthoma elasticum of the skin. The degeneration of the elastic tissue is similar to that found in the skin in pseudoxanthoma elasticum.

This theory seems best to explain the peculiar appearance of the fundus known as "angioid streaks of the retina" and its unusual association with the rare disease of the skin, pseudoxanthoma elasticum.

CONCLUSIONS

1. Angioid streaks of the retina appear to be situated in the choroid, and therefore should be called angioid streaks of the choroid.

2. The association of pseudoxanthoma elasticum and angioid streaks of the choroid occurs too often to be explained by chance association.

3. The occurrence of angioid streaks of the choroid is best explained in the following manner: Short posterior ciliary veins passing through the sclera in an anomalous manner become thrombosed mechanically by the increase in the fibro-elastic tissue of the sclera, resulting in the appearance of hemorrhages, exudates and streaks corresponding to the vessels involved.

Miss Lillian Kennedy prepared the drawings of the fundus; Dr. F. P. Calhoun allowed me to report case 2; Dr. Jack Jones and Dr. Herbert Alden made the reports on pseudoxanthoma elasticum, and Dr. Everett L. Bishop made the pathologic report on the skin.

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ABSTRACT OF DISCUSSION

Dr. W. E. Fry, Philadelphia: The association of two disease entities, one of the eye and the other of the skin, each of which is rare in its respective field, is interesting, both from the analogies that can be drawn and from the pathologic examinations that have been made. It is of particular interest that most of the recently reported cases of angioid streaks of the retina have also shown pseudoxanthoma elasticum, and this has occurred with a frequency that appears more than merely coincidental. Of the sixteen more recently reported cases, twelve exhibited this association. These twelve cases include three reported by Gronblad,

four by Marchesani and Wirz and five by Clay. The first of these cases was reported by Gronblad, unless we include, as do Marchesani and Wirz, a case report in the dermatologic literature by Darrier in 1896. This was a case of pseudoxanthoma elasticum, and at that time there were no ocular symptoms, and no ocular examination was reported. Later, in 1902, a sudden loss of vision developed, which was found to be due to a macular retinochoroiditis. Marchesani and Wirz point out that in all probability the condition was a late manifestation of angioid streaks. In connection with the aforementioned cases, the report by Griscom is of interest. The case was that of a colored man, who, in addition to the angioid streaks, exhibited a peculiar, irregular, slate-colored pigmentation on the skin of the forehead. This was reported to be chloasma, a condition which, although not definitely classified, was supposed to be a pigment proliferation due to neurotrophic influences. Through the courtesy of Dr. Griscom, I have had the opportunty of having this patient reexamined with the view of determining the presence of pseudoxanthoma elasticum. Dr. Gilman, who made the examination, stated that there was no evidence of a cutaneous lesion of that type. It has been possible to review the case history of one of the two patients who formed the basis for the report on angioid streaks by Holloway. This patient had been hospitalized and thoroughly studied on several occasions. In this instance, no cutaneous condition was found.

There are certain differences in the etiology of angioid streaks and of pseudoxanthoma elasticum which it may be well to review at this time. The ages of the patients with the latter condition varied from 7 to 74 years in the case reports reviewed by Thorn and Goodman. In four cases, in which the age of onset was stated, it was given as earliest childhood, and in eight other cases, as 10, 16, 18, 20, 38, 46 and 54 years, respectively. In only two instances (18.3 per cent) was the age of onset over 40. In the review of angioid streaks by Holloway, the age of occurrence was under 20 in four instances, from 20 to 40 in sixteen instances and over 40 in thirty-two instances (53.3 per cent). In spite of the short series compared, there is a well marked difference in the age group involved. In regard to sex, of the twenty cases reported by Thorn and Goodman, fourteen, or 70 per cent, were in females, and six, or 30 per cent, in males. In the case reports of angioid streaks reviewed by Holloway, thirty-five patients, or 62.7 per cent, were males, and twenty-one, or 37.3 per cent, were females. Here again there is a difference in the proportion of the sexes involved. In both conditions more than one member of the family may be affected, although there is no marked familial tendency. Both conditions are free from subjective symptoms in the early stages. It appears, therefore, that pseudoxanthoma elasticum is a disease of youthful and adult persons of both sexes, with a preponderance in females, and that angioid streaks is a disease of persons of middle age and beyond, with a preponderance in males.

Despite the foregoing differences, the occurrence of two such rare disease entities in the same person allows interesting etiologic speculations. Undoubtedly, the primary change in pseudoxanthoma elasticum is in the elastic tissue of the skin. Marchesani and Wirz believe that in angioid streaks the primary change is a similar degenerative process of the lamina vitrea of the choroid. The lamina vitrea is but one of the glass membranes of the eye, and there is no reason why one should be involved to the exclusion of the others. Such an etiology gives prominence to the theory advanced in 1917 by Kofler, who attributed the lesions to fissures in the membrane of Bruch. On the other hand, Dr. Clay believes that the angioid streaks are the result of a thrombosis, which, in patients with pseudoxanthoma elasticum, is dependent on a degeneration of the elastic tissue of the sclera. Marchesani and Wirz also point out that small hemorrhages appear spontaneously in the skin, and that they directly parallel the hemorrhages seen in the oculi of the fundus.

I was not certain whether reference was made to the paper on the histologic findings in a case of angioid streaks of the retina presented before this Section in 1928 by Verhoeff. It is, I believe, distinctly worth while to point out certain differences in the findings recorded in that instance and the histologic findings in pseudoxanthoma elasticum. In the case of angioid streaks, there was found a marked fibrosis within the choroid, to such an extent that the normal structure of the middle layers of the choroid were entirely replaced by fibrous tissue with numerous connective tissue cells, over a considerable portion of the posterior pole of the eye. In the reports on pseudoxanthoma elasticum, there is no mention of the proliferation of connective tissue or of the formation of fibrous tissue. Concerning elastic tissue changes, Verhoeff's report repeatedly stated that the membrane of Bruch was intact, whereas in pseudoxanthoma elasticum there is an extreme degeneration of the elastic tissue of the skin. The streaks in the ocular condition were shown to be the result of a cicatricial contraction of the fibrous tissue, which replaced the deeper layers of the choroid. On the other hand, Macleod states that the nodules in pseudoxanthoma elasticum were due to the presence of a mass of swollen and fragmented elastic tissue fibers situated in the reticular part of the corium. The color of the streaks in the ocular disease was due to a folding of the pigment layer of the retina, and the color in the cutaneous disease, to the degenerated elastic tissue. Verhoeff's report stated that the blood vessels were greatly reduced in number, that they were especially small and scanty in the middle layer of the choroid and that where present, they consisted almost exclusively of veins. Dr. Clay did not observe any marked vascular changes, but the report of Marchesani and Wirz states that there was a secondary reactive process in the vessels, which proliferated and became abnormally full and exhibited changes in the walls of the vessels.

In two of the cases reported by Dr. Clay the association of angioid streaks with senile elastosis is noteworthy in view of the opinion expressed by Weidman that histologic observations in themselves do not constitute an adequate basis for a differential diagnosis between pseudoxanthoma elasticum and senile elastosis.

It appears, therefore, from the comparisons noted, that in spite of the relatively large number of case reports that have recently been made which exhibit both angioid streaks and pseudoxanthoma elasticum, the resemblance is superficial, and that real differences occur in the age groups and sex proportions of the patients involved, as well as in the histologic and pathologic findings recorded. Hence, ophthalmologists should be slow in drawing conclusions from the analogies that can be made between these two conditions.

Dr. Arthur J. Bedell, Albany, N. Y.: The theory that Dr. Clay presented is of interest, but I am not convinced that it explains satisfactorily the appearance of the fundus in these cases.

By means of stereoscopic photographs it is possible to study the dark streaks with greater understanding than by simple examination of the fundus.

Dimmer and Pillat, in their atlas, "Photographischer Bilder des menschlichen Augenhintergrundes," showed several types of angioid streaks, and it is difficult to conceive that the lines portrayed on their plate 61 are the result of thrombosis of vessels. Their plate 62 is more of the type I have seen and is of the kind shown in Dr. Clay's drawings.

I should like to ask Dr. Clay whether he has ever seen the short posterior ciliary veins follow a course similar to the streaks in the photographs that I showed on the screen.

I should also like to know whether he has ever seen a thrombosed vessel with such a ragged outline. Angioid streaks certainly are flatter, wider and more

irregular than venous channels. They do not seem to be made up of unconnected branches, but rather of heaped-up pigment. The more I examine these cases the more I tend to think that the dark lines are migrated pigment. They remind me of the débris-strewn banks of a river that has subsided from flood height. Frequently, as Dr. Clay has clearly stated, there is a definite choroidal absorption. Other observers have recorded a similar appearance, and it is evident in the photographs.

Whenever it is possible to see the choroidal vessels, the retina is thin, and we know that the channels are practically never found as radiating lines, but always have a wavy contour. As far as I have been able to discover in checking over a great many thousand photographs, the suggestive or even diagnostic concentric ring or arc about the disk is never found except in angioid streaks. When the choroid and surrounding retina are involved in the macular exudative inflammation, one can eventually, when the disease has become quiescent, trace the retinal vessels over the distorted choroidal channels, and yet I have never seen irregular streaks or radiating lines simulating angioid streaks in appearance.

As I am skeptical regarding thrombosis as a disease of the blood vessels, I shall be glad to have Dr. Clay explain these points and convert me to his view.

Dr. Jack Jones, Atlanta, Ga.: Pseudoxanthoma is rather more rare to the dermatologist than are angioid streaks to the ophthalmologist. The first three cases I had showed an association of the two conditions, and at that time I thought it must be a constant finding, owing to the fact that the two diseases, which are rare, were found in the only three cases I had seen. However, as I went further, I found two other cases that showed no such association.

Pseudoxanthoma occurs primarily in the flexures of the body. Clinically, the condition resembles scar tissue, with small yellow tumors thereon. Most patients notice the condition, but simply consider it a scar and pay no attention to it. I do not think that any dermatologist would recognize such cases without the ophthalmologist's help. Few men in dermatology have seen cases of pseudoxanthoma. It was my good fortune to see one before I started to follow this series. I have a few slides that demonstrate the pathology of the condition.

I have been trying to understand the etiology and pathology of pseudoxanthoma, and after studying the literature and making some investigations, I have come to the conclusion that they must be associated with senile changes in some way. The first slide shows a condition similar to pseudoxanthoma; the second one shows senile elastosis in a patient 75 years of age. Clinically, the conditions are markedly different.

The main process is a breaking down of the structures and the formation of elastic tissue. For that reason, I consider pseudoxanthoma elasticum a manifestation of a senile change in the skin. Why early cases show this breaking down I have not been able to explain. When that explanation has been reached the explanation for most of these cases will probably also have been reached.

Dr. Derrick T. Vail, Jr., Cincinnati: At the 1928 meeting of this Section, in discussing Verhoeff's paper on the same subject, I presented a patient with angioid streaks of the retina, and at that time expressed the opinion that Verhoeff's theory of pathogenesis of this disease more satisfactorily explained the origin of the streaks than any other. With all respect to Dr. Clay, I still hold that opinion. The name which Verhoeff gave the pathologic picture in his case, fibrosis choroidae corigans, is most descriptive. The fibrosis of the choroid, whatever the cause, by contraction, causes folds to appear. The most likely place in the fundus is around the disk in a radiating fashion, since here the membrane is most firmly attached. That the process is limited to the choroid can be ascertained clinically by the

Gullstrand binocular ophthalmoscope. The hemorrhages in the subchoroidal space are apparently the primary lesions. The streaks and macular involvement are secondary manifestations. The macular lesion is probably the result of extravasation of blood, as suggested by the yellow tinge, or lymph in the subchoroidal space or immediately under the retina in or near the macular region, at least in the posterior pole of the eye, which is temporal to the disk.

That a thrombotic process limited to a bilateral anomalous collaret of veins around the disk can be the fundamental lesion and the cause of angioid streaks is inconceivable to me. Dr. Bedell's cases and my own, as well as many other reported cases, show a characteristic collaret. Dr. Clay's paintings and drawings do not reflect the typical picture, and there is a question in my mind whether some of them, at least, are true angioid streaks.

Dr. Walter B. Lancaster, Boston: Dr. Clay deserves a great deal of credit for bringing together such an unusually large series of this rare disease and for emphasizing again the connection of the disease with this peculiar cutaneous condition. As he says, the absence of definite, authentic histologic examination in such a case invites speculation, and so he speculates on the possible nature of the disease. Speculation, however, invites and even demands criticism—the criticism that I should like to offer here.

We are asked to assume the existence of vessels not occurring in the normal eye. Furthermore, we must assume that the abnormal vessels become the subject of thrombosis. Now, thrombosis, when it finally blocks a vessel, is an acute process and produces marked symptoms and changes. But in angioid streaks the onset is so slow and almost imperceptible that the condition is rarely discovered until it is far advanced. Moreover, as Dr. Bedell clearly indicated, the shape of the streaks, their irregular outline, does not correspond to the outline of a vessel with thrombosis. Then, hemorrhages seem to be a feature of the disease, recurring throughout its course and not merely at the beginning.

On the other hand, Verhoeff's case also required certain assumptions. It is not free from objections. The objections are that it was not examined before enucleation, and that the other eye did not show angioid streaks. Against this we must place the striking fact that the histologic report of the condition satisfactorily explains all the symptoms found in angioid streaks. It is rather difficult, in the face of these convincing findings, to reject the diagnosis. I admit, however, that it is not absolutely conclusive. Dr. Verhoeff has loaned me two or three slides.

The first slide shows that the choroid has become largely cicatricial tissue (fibrosis), and the resulting contraction has produced these folds in the adjoining retinal pigment layer. The folds vary a good deal in height, and some of them are more or less flat, which explains the variation of width seen in the streak. This is a characteristic feature of the angioid streaks and is not explained in the theory of thrombosis. There is one streak that is bent far over. The second slide shows, on one side of the field, almost complete atrophy of the choroid. There is a hemorrhage, which is a prominent feature of the disease. The third slide shows a piece of the retina from which the celloidin was dissolved, a picture taken of the surface of the retina as it would be seen with the ophthalmoscope and showing the streaks as they actually occurred in this patient. It seems to me by no means a poor representation of angioid streaks.

The fourth slide shows, by way of contrast, a collection of pigment of a different type. This is the condition found in striate choroiditis; pigmented lines occur when there has been detachment of the choroid which has become replaced. Compare it with the striae found in angioid streaks. In this type there is a deposit of pigment, and in the angioid streaks, a folding of the pigment layer.

Dr. Grady E. Clay: I appreciate the discussion. I wish to apologize for failing to mention Dr. Verhoeff's report of a case of angioid streaks before this section, but it was an oversight on my part. His case has been mentioned here, but I do not think that it can be considered as an authentic case of angioid streaks, since the eye was not examined with an ophthalmoscope prior to enucleation and, previous to enucleation, there were trauma, a corneal ulcer, secondary glaucoma with an iridectomy and loss of vitreous. Certainly, such an eye might present any pathologic picture, and, too, the opposite eye in this patient did not present angioid streaks.

Dr. Bedell asked, "If the streaks are blood vessels, why do they have such a peculiar appearance?" If one will observe the deeper retinal veins, it will be seen that their borders have a serrated appearance, as is noted in angioid streaks, and along these thrombosed vessels there must be some hemorrhages, which likewise give it the unusual appearance. He asked whether I have seen a short posterior ciliary vein. I have not, and so far as I know there have been only two reports of such veins in the literature. I still think that the occurrence of angioid streaks of the retina can be best explained by thrombosis of the short posterior ciliary veins.

CONGENITAL BILATERAL PALSY OF THE ABDUCENS

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AND
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CLEVELAND
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COLUMBUS, OHIO

A girl, aged 5 years, had a nonconcomitant convergent strabismus due, apparently, to a bilateral palsy of the abducens. Neither eye could be abducted beyond the midline, and adduction, although not measured instrumentally, seemed to show some deficiency of the interni. Both facial nerves were intact, and a general physical examination revealed nothing out of the ordinary.

Although a letter was written to the obstetrician, there was no information about the birth of the child available except from the mother, who stated that there was nothing unusual in the delivery so far as she knew. There was one brother two years younger than the patient who had had some thoracic difficulty when quite young and was seen in the free clinic at Cleveland City Hospital, where an x-ray plate was reported as showing an enlarged thymus gland. This child was seen again later, and, as there had been no change in the shadow on the second plate, it was decided that the condition was a thickening of the peritracheal lymph nodes.

For cosmetic purposes, the parents were anxious that something should be done to correct the deformity of the patient. A bilateral resection of the externi with some recession of the interni was performed under gas-ether anesthesia. The child did not take the anesthetic well, and, just as the operative work was completed, she ceased breathing. (An hour and a half was spent in trying to resuscitate her, but without success.)

At postmortem examination, the observations reported by the pathologist included a thymus weighing 36 Gm. overlying the great vessels and the heart to a point considerably below the auriculoventricular line. The heart and the vessels were normal, except that they were disproportionately small for the child's size and age. When the brain was removed, no trace of either sixth nerve could be discovered. The entire specimen was sent to Prof. Ernest Scott of the department of pathology at Ohio State University for microscopic study of serial sections of the nuclei. The observations of one of us (Dr. Graves) during this study of the brain were as follows:

A study of the brain in the pathologic laboratory showed that the abnormalities were confined to the medulla and the pons. External observation revealed the entire absence of the sixth nerves (fig. 1). This promptly suggested a microscopic examination to yield additional evidence as to the cause of the absence.

Careful study of the microscopic sections (serial sections, 25 microns in thickness, prepared by the Weigert technic) indicated that there were decided abnormalities in the sixth nuclei, the nuclei being of diminutive size, with few cell nuclei.

Read before the Ophthalmic Club of Cleveland.

These diminutive sixth nuclei were about 1 mm. in diameter and were confined within an area bounded by the genu of their respective facial nerve. The genu on each side was also smaller than that of the normal brain, which is usually 1.7 mm. in diameter, according to Sabin.[1] In addition, the nuclei were not well defined and not quite in their normal position. The nuclei were above the planes of the genu in their whole extent (fig. 2), not at and below the planes, as was found in the normal brain stem (fig. 3). There was no suggestion of a deviation from the normal in the shape of the genu, the cephalad embryonic shift of the diminutive sixth nucleus or the caudal and ventrolateral shift of the facial nucleus.

Fig. 1.—The ventral view of the brain of a 5 year old girl with bilateral internal strabismus, showing the absence of the sixth nerves. One-half reduction.

Descending from the region of the diminutive sixth nuclei were seen a few scattered fibers (fig. 4, see arrows). None of these fibers could be seen with the unaided eye from an inspection of the sections (fig. 2). The fibers were in strands of two or three and extended only a short distance into the pons. No fibers were ever seen which reached from the sixth nucleus to the medial lemniscus; the usual extent was one fourth or one fifth of this distance. In some sections,

1. Sabin, F. R.: An Atlas of the Medulla and Midbrain, Baltimore, The Friedenwald Company, 1901, p. 54.

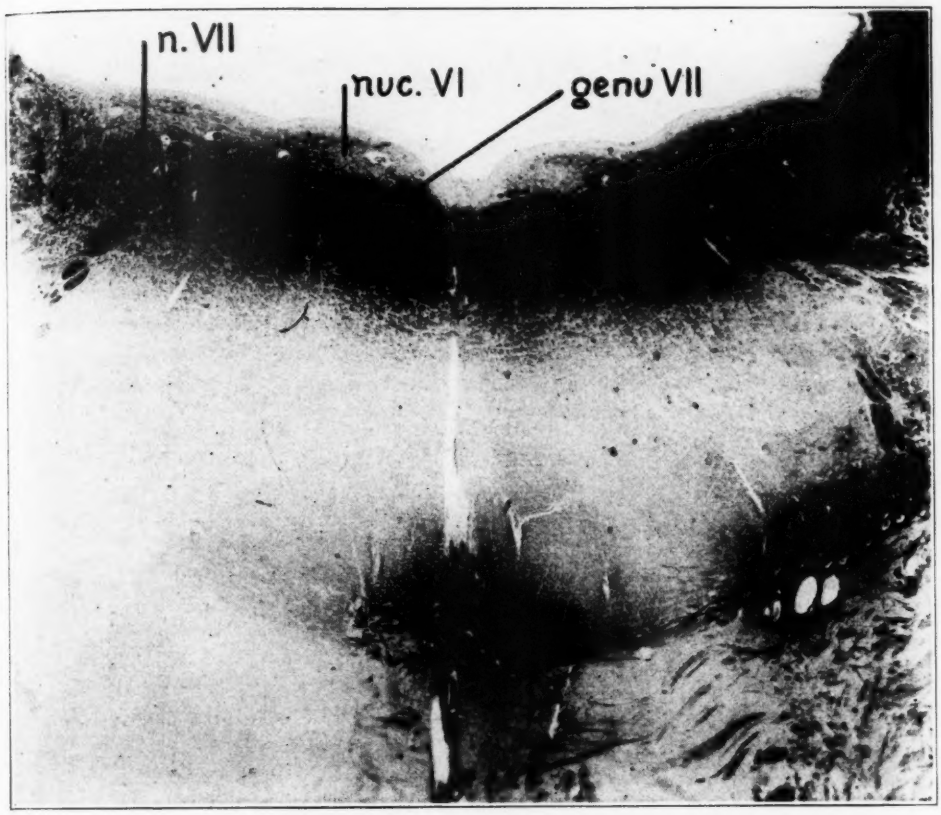

Fig. 2.—A section through the diminutive sixth nuclei, showing their abnormally high position above the level of the genu and the absence of the sixth nerves.

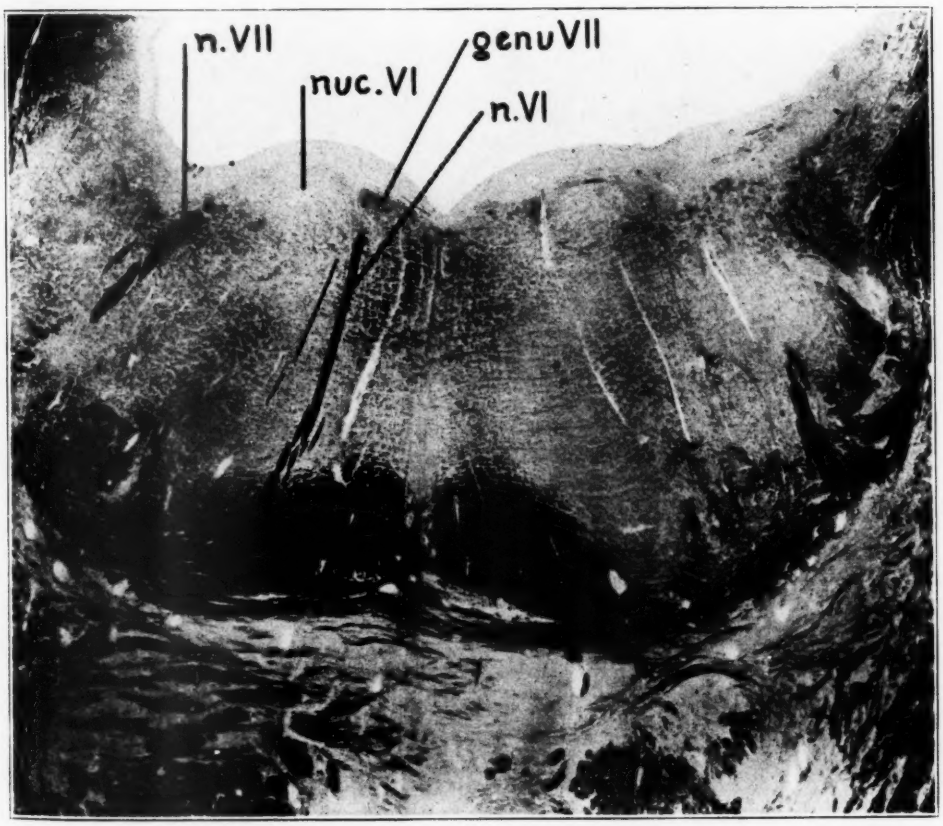

Fig. 3.—A section through the normal sixth nuclei, showing the position to be at and below the level of the genu. The sixth nerve is shown on one side.

the ends of these fibers did not seem to be pointing in a ventral direction, but turned to point laterally. These few fibers were directed as the sixth nerve would be if present and in normal proportions, that is, downward, ventrally and from just lateral to the genu. The possible termination of these fibers could not be determined by careful examination of the sections. In certain slides (fig. 4, under white half-moons) a few isolated triangular cells, similar to the ones of the nuclei, were found along the course of these fibers.

Fig. 4.—The few scattered descending sixth fibers just lateral to the genu of the facial nerve. The arrows point to the probable descending sixth nerve fibers. Occasional triangular cell nuclei (under the white half-moons) are scattered along the descending sixth nerve fibers.

In the same sections through the sixth nucleus, there were found perhaps 50 nuclei, of which 10 were triangular and deeply stained, as is characteristic of the nuclei of the normal sixth nucleus. The majority of sections through the sixth nucleus showed, however, a total of less than half of the normal number of ganglion cells, the usual average being from 80 to 100 triangular nuclei, found in the center of the normal sixth nucleus. The largest number of these cells were faintly

stained and contained round nuclei (fig. 5), which are seldom seen normally. The cells of the diminutive nucleus showed the ganglion cells to be densely packed in some of the sections, which is in marked contrast to the widely placed cells of the normal sixth nucleus. Other sections presented only a few cells of either type.

Pathologically, there appeared to be little evidence of fibrosis in the neighborhood of the sixth nucleus. It may be mentioned, however, that the light area above the location of the diminutive sixth nucleus was perhaps more richly sup-

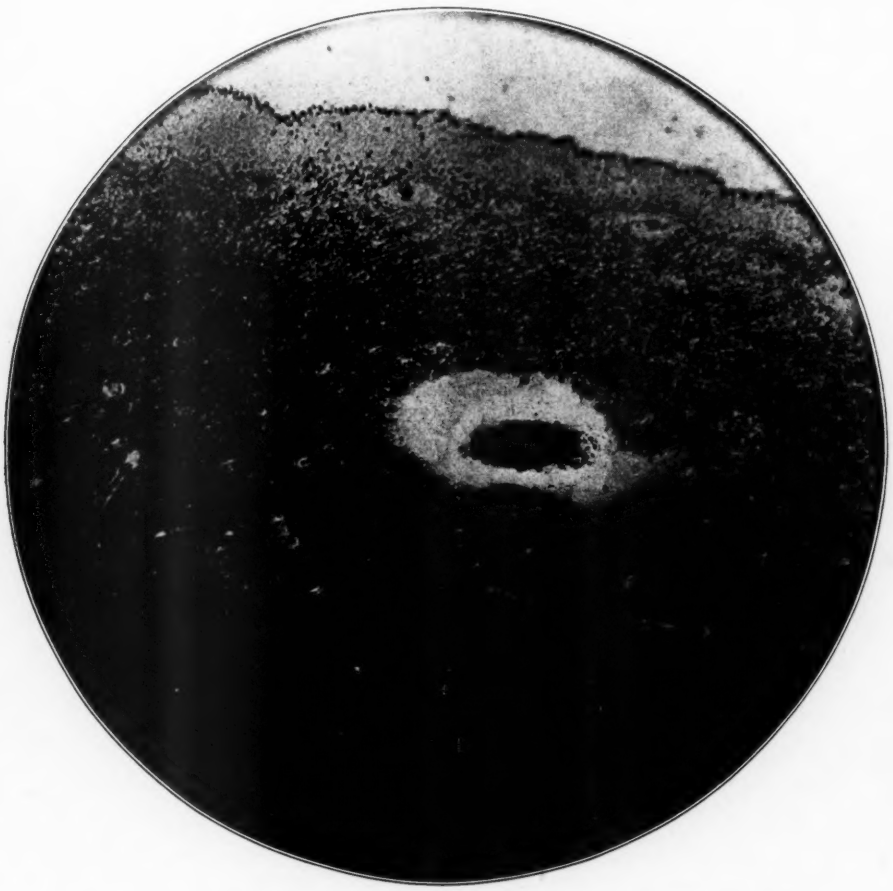

Fig. 5.—The diminutive sixth nucleus, to show the types of cell nuclei.

plied with blood vessels than is the corresponding area of the normal brain. This, nevertheless, does not suggest a definite pathologic change.

The surrounding nuclei seemed to be of normal size and of normal shape. Of the nuclei near the midline, for example, the twelfth nucleus was the usual distance from the genu of the facial nerve (about 1 mm.).

An accompanying abnormality was noticed in the immediate vicinity of the small sixth nucleus. There appeared to be an aberrant fiber tract (fig. 6 *a*, *b* and *c*, *tr.*) just medial to the nucleus, which, when traced caudally, was found to be connected with the nucleus eminentia teres. A description of this nucleus and its fiber tract will be detailed.

The fibers of the nucleus eminentia teres gathered together in bundles at first on their respective sides (fig. 6 *a, tr.*), but as they passed cephalad they united into a single median bundle (fig. 6 *b, tr.*). This bundle of fibers occupied a special median elevation in the floor of the fourth ventricle, not seen in the normal brain stem. In fact, the nucleus eminentia teres appeared abnormally long, extending as far cephalad as the beginning of the genu of the facial nerve. As the nucleus eminentia teres ended, the bilateral fiber bundles increased greatly in size. This fiber tract extended cephalad to the level of the superior limit of the genu of the facial nerve, where it again divided into multiple bilateral bundles (fig. 6 *c, tr.*).

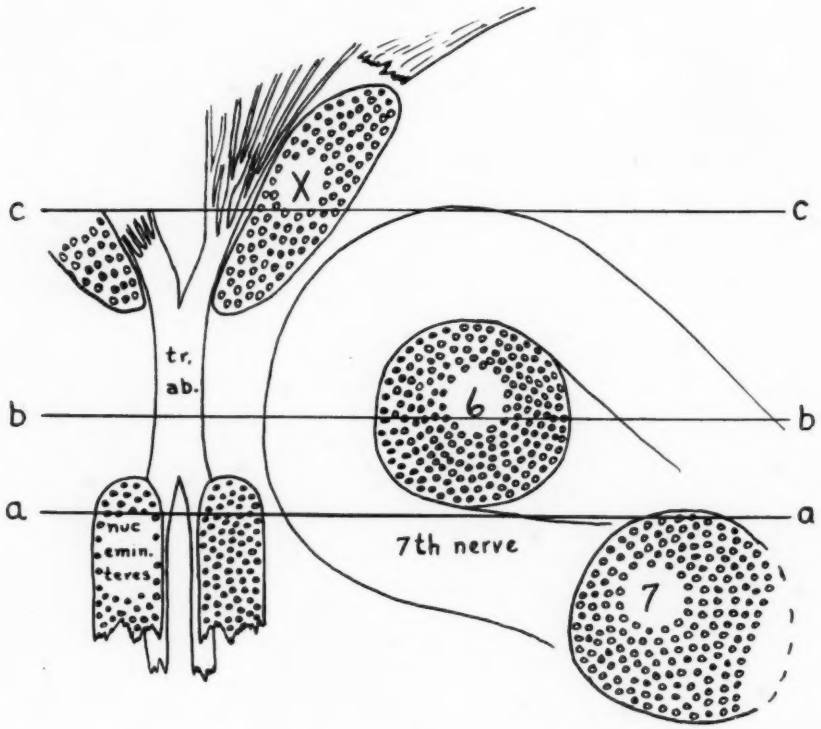

Fig. 6.—A diagram of the aberrant median fiber tract, with photographs at the levels *a, b* and *c* of the diagram. In *a* is shown a section through the nucleus eminentia teres. The aberrant fiber tract is shown ventromedial to the nuclei. In *b* is shown a section through the center of the sixth nuclei and genu. The aberrant fiber tract is in a single bundle beneath a median ridge in the floor of the fourth ventricle. In *c* is shown a section through the superior limit of the facial genu. The aberrant tract is ventromedial and ventral to the nucleus.

This division of the aberrant fiber tract (fig. 6 *c, tr.*) was associated with a small nucleus dorsolateral to it and dorsomedial to the ascending fibers of the genu of the facial nerve. It may be that this small nucleus was an isolated part of the nucleus eminentia teres, for its position and the character of its cells were the same, although it might have been a detached part of the sixth nucleus, which, however, is less likely. There was a possible connection of the tract fibers with

Figure 6

this nucleus, although the great majority, if not all, of them extended further cephalad, to disappear entirely at the level of the lateral shift of the medial longitudinal lemniscus. The fibers seemed to disappear laterally into the light areas immediately beneath the floor of the fourth ventricle at this place.

In summary, the evidence presented by the slides suggests that the diminutive size of the sixth nucleus is due to a congenital defect in development. The accompanying abnormality of the median fiber tract from the nucleus eminentia teres strengthens such a hypothesis. The inability to trace the few scattered fibers of the sixth nucleus to their usual exit from the brain substantiates the autopsy observation that the sixth nerves were absent on gross observation.

COMMENT

This case is exceedingly interesting and instructive from two standpoints: (1) from the opportunity for study under most favorable circumstances of the histopathology underlying a congenital bilateral abducens palsy and (2) from its association with a so-called "status thymicolymphaticus."

Harold Gifford,[2] in 1926, presented a complete and lengthy review of the literature on the etiology of congenital palsies of the abducens. Most of the paper is devoted to monolateral paralyses, which, as a rule, are unassociated with other deformities and palsies and, in the main, are considered as injuries sustained at birth. Of the forty-three cases of bilateral palsies reported, more than one-third showed some other deformity, such as limitation of adduction, enophthalmos, paralysis of one or both facial nerves or of the tongue, harelip and cleft palate and deformities of the chest, fingers, hands or feet.

Very few bilateral cases have come to autopsy, so that central changes, if present, have not often been recorded. An article by Heubner [3] was the only one available. His work coincided with work done in the case under discussion, his plates of the sections of the brain being absolute proof of the "marked hypoplasia of the nuclei" (the seventh and eighth nerves were also involved in his case).

It is quite evident that a unilateral palsy may be due to a local injury, such as pressure from forceps at delivery or otherwise during birth, or it may have a central origin, as in a small pontile hemorrhage. The fact that it is rarely accompanied by other changes would argue for a local rather than a central origin. Bilateral palsy, on the other hand, would rarely be local, and the fact that a third of the reported cases were accompanied by paresis of other nerves, notably the seventh, the nuclei of which are contiguous, or by some type of deformity would argue for either a central lesion or the presence of

2. Gifford, Harold: Congenital Defects of Abduction and Other Ocular Movements and Their Relation to Birth Injuries, Am. J. Ophth. **9**:3 (Jan.) 1928.

3. Heubner: Bilateral Abducens Palsy with Paralysis of VIII and Left Lower VII, Charité-Ann. **25**:112, 1900.

some underlying condition that tends to arrest development. Cases associated with paresis of one or both facial nerves *only* might certainly be due to a small pontile hemorrhage sustained at birth. On the other hand, they could also easily be due to an isolated deficiency of nuclear development. The cases associated with involvement of the facial nerves *and* deficiencies elsewhere, such as ocular colobomas, cleft palate, harelip and deformities of the fingers and toes, would likely be caused by developmental defects, due not to injury, but rather to embryonic deficiencies.

The second interesting point in the case reported is its association with an enlarged thymus with its train of cardiovascular changes. It is a well established fact that patients with persistent thymus are prone to show developmental defects. Greenthal [4] found that thirty-three of ninety cases showed congenital deformities of some kind. In Cooperstock's [5] series of 335 cases, 112 showed defects, most of which were cleft palates or harelips.

There is some dispute as to what constitutes a really enlarged thymus. Scammon recently, after examining 1,074 children, expressed the following opinion: "The new-born thymus weighs fourteen grams and increases gradually to a maximum of thirty-five grams until puberty when it gradually indergoes involution." On the other hand, Harris [6] of Richmond said that anything over 10 Gm. is pathologic. When one realizes that most of these measurements are guessed at from the size of the thymus shadow on an x-ray plate and realizes the chance for error, the difference of opinion is readily understood. As a matter of fact, it is probably not just the size of the thymus that is to be considered, but the amount of defective development associated with it.

The function of the thymus is not well understood. That it bears some relation, and a close one, to thyroid function is shown by the fact that a large thymus is almost invariably associated later with exophthalmic goiter. That it bears also some relation to the pituitary gland is apparent from the fact that cases of status thymicolymphaticus and thymic asthma almost always show evidence of genital hypoplasia and adiposity. In other words, the thymus seems to have an exactly opposite effect to that of the developing triad, thyroid, pituitary and pineal glands. From this has been ascribed to it an "inhibitory function," its activity during the growing period of a child's life holding back the developing characteristics of the thyroid, pituitary and pineal

4. Greenthal, Roy: Incidence of Thymic Enlargement Without Symptoms in Infants and Children, Am. J. Dis. Child. **24**:433 (Nov.) 1922.

5. Cooperstock, M.: Present Concepts of Enlarged Thymus and Status Thymico-Lymphaticus: A Review of a Decade's Experience, J. Michigan M. Soc. **29**:21 (Jan.) 1930.

6. Harris, W. L.: South. Med. & Surg. **92**:78 (Feb.) 1930.

glands. This inhibitory function is offered as an explanation of the hypoplasias and deficiencies so commonly associated with its hyperplasia.

The complete absence in the case reported of both abducens and their diminutive sixth nuclei and the presence of a marked thymic hyperplasia with its well known train of cardiac and vascular hypoplasias lead one to the thought that perhaps bilateral congenital palsy of the external recti may be only another of the hypoplasias dependent on the thymic disturbance, rather than the result of an injury or hemorrhage sustained at birth. At any rate, it should make one careful how one operates in these cases without careful investigation of the thymus beforehand.

NEVUS FLAMMEUS OF THE FACE AND GLOBE

ASSOCIATED WITH GLAUCOMA, VASCULAR CHANGES IN THE IRIS AND A CALCIFIED VASCULAR GROWTH IN THE LEFT OCCIPITAL LOBE OF THE BRAIN, WITH RIGHT HOMONYMOUS HEMIANOPIA

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The infrequency of the occurrence of the associated condition of nevus flammeus with increased intra-ocular tension and the extreme rarity of the presence of a calcified vascular growth in the occipital lobe, with resulting right homonymous hemianopia, prompt me to record the following case as one that may prove of interest.

REPORT OF CASE

History.—B. M., aged 26, applied for treatment at the Knapp Clinic on Dec. 15, 1931, for pain over his left eye, with blurring of vision for the preceding three weeks. The left side of his face presented a nevus flammeus, extending from the hair to the lips, down the median line of his forehead and nose and outward on a level with his lower lip, reaching to the lobe of the left ear below and to the hair on the left side of his head. He also had vascular changes on his hard palate and on the left side of his throat. There was increased vascularity of the conjunctival, circumcorneal and scleral vessels. Six years previously he had received treatment with radium for the nevus, which extended over a period of one year, with slight improvement; apparently no ocular examination was made at that time.

Examination.—Vision in the right and left eyes was 20/20. Motility was normal; the pupils measured 4 mm.; the reaction to light was somewhat sluggish; the cornea was clear and was 11 mm. in diameter. The anterior chamber was deep. Tension as measured with the Schiötz tonometer was 45 in the left eye and 13 in the right. The fundus of the left eye showed glaucomatous cupping, with the vessels pushed to the nasal side. There was some dilatation of the retinal veins in the extreme periphery of the fundus, especially superiorly and nasally. There was pallor of the disk of the right eye, with no cupping or changes in the vessels of the fundus. The exophthalmometer showed 20 in the right eye, and 20 — 110 in the left. The slit lamp demonstrated dilated vessels on the left iris, especially clumps of vessels in the periphery near the angle.

Slit lamp examination (Dr. Newman) showed: The entire construction of the iris was wanting. The pigment was scarce, and the fibrillary structure of the trabeculi was rather loosely knit. This enabled the observer to view the vessels in the trabeculi; normally they are not visible. In places, the fine layer of connective tissue surrounding the vessels was seen. The vessels were visible

Presented before the Ophthalmological Section of the New York Academy of Medicine, Jan. 18, 1932.

throughout the entire circumference of the superficial mesodermic layer of the iris, as branches of the circulus iridis minor, thinning out as they reached the periphery, being more prominent in some areas than in others.

The circulus iridis minor, which is the vascular circle of the collaret and at the same time the free border of the superficial mesodermic layer of the iris, as a rule is not seen as a true vascular circle. In this case, however, the observer could follow the vessels around its entire circumference.

Between 12 and 3 o'clock, two markedly dilated, tortuous vessels, probably veins, were visible in the deeper stroma. The first ran from the border of the iris, just behind the retinal pigment layer, at about 12 o'clock, directly upward, to be lost in the angle of the anterior chamber. The other commenced immediately below the first and ran obliquely outward at about 2 or 3 o'clock, and also terminated in the angle of the anterior chamber. In this instance, however, the termination was in the form of spiral loops. Also on the nasal side at 9 o'clock two prominent vessels were evident with the gonioscope, one overlapping the other and terminating deeper in the angle than the loop on the temporal side.

Fig. 1.—Photograph of the patient, showing the nevus of the face and globe.

With proper illumination the sphincter was visible. The pars iridica retinae appeared normal in consistency and pigmentation.

The fluorescein test (internal administration) within three hours gave a marked greenish color to the aqueous in the left eye, on the side with the nevus, and showed no staining of the aqueous in the right eye, thus showing an increased permeability of the vessels in the left eye, producing a "plasmoid aqueous," as termed by Duke-Elder,[1] and causing a diminution in the excretion of aqueous, with an increase in the intra-ocular tension.

Examination with the gonioscope (Troncoso[2]) showed the angle of the iris to be free from adhesions in its entirety. Dilated vessels on the left iris were visible at 2, 6 and 9 o'clock. The latter were not visible with the slit lamp, on account of being in the extreme angle of the iris and beneath the opaque portion of the limbus corneae. Tension as measured with the Schiötz tonometer was 15 in the right eye and 35 in the left at time of the examination. Apparently there were no adhesions in the angle of the iris to account for the ocular hyper-

1. Duke-Elder, W. S.: Recent Advances in Ophthalmology, Philadelphia. P. Blakiston's Son & Co., 1927.

2. Troncoso, M. U.: Am. J. Ophth. **8**:433, 1925.

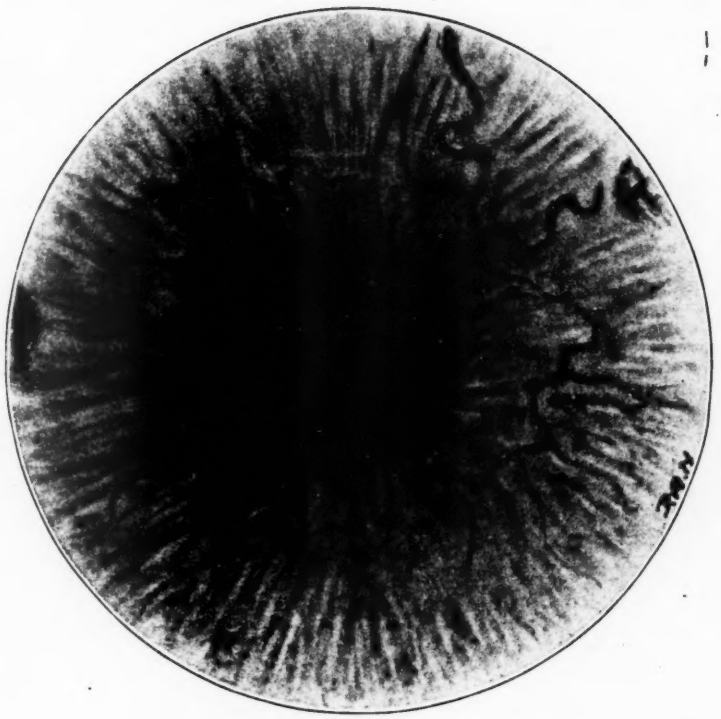

Fig. 2.—Drawing showing dilated vessels on the left iris, forming clumps in the periphery, and a complete circulus irides minor.

tension, such as were thought to produce it in some of the other cases reported. However, in this case, as in one other case of nevus examined, there were dilatation of the capillaries of the iris and an increased permeability of the walls of the vessels, as shown by the fluorescein test. In either one or both of these conditions one may find ocular hypertension, owing to an increased density of the ocular fluids, which tends to diminish their outflow. The visual fields revealed a right homonymous hemianopia with an additional contraction of 20 degrees in the temporal field of the left eye. (The patient had not noticed any defect in his visual field until tested; see fig. 3.)

With the use of pilocarpine, a 2 per cent solution, tension was controlled within normal limits. When the patient was ill with influenza, for two weeks, he discontinued the pilocarpine; the tension immediately rose again to 35 in the left eye and 17 in the right, which fell to normal under the influence of miotics.

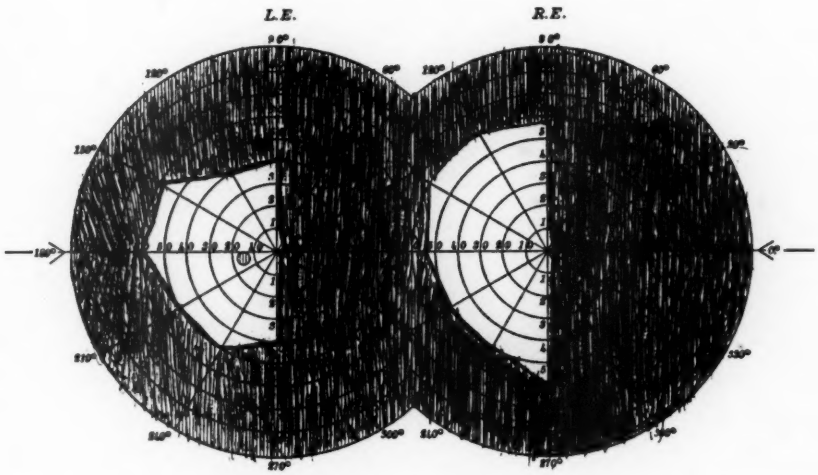

Fig. 3.—Visual fields. Test object 1 cm. white, showing right homonymous hemianopia.

Physical examination at Roosevelt Hospital on Feb. 2, 1932, showed: There was much dentistry, with capped teeth. The chest, heart, lungs, abdomen and extremities were normal. The blood pressure was 115 systolic and 70 diastolic. The reflexes were normal. The Wassermann reaction of the blood was negative. The urine was normal. The blood urea nitrogen was 15.8 mg. per hundred cubic centimeters; the blood sugar, 134 mg.

Roentgen examination of the skull by Dr. Boone of Roosevelt Hospital "demonstrated a marked irregular shadow of increased density in the left occipital lobe adjacent to the tentorium. The diploic veins are somewhat tortuous and well marked. There is no evidence of increased intracranial pressure, sella normal, no erosion of clinoid processes. The appearance of the films is that of calcification in a new vascular growth of the brain, probably a hemangioma."

In 1927, Dr. A. Knapp[3] presented a report of an interesting case of glaucoma in a patient with a generalized vascular nevus of the skin

3. Knapp, Arnold: Glaucoma in a Generalized Vascular Nevus of the Skin, Arch. Ophth. **57**:219 (May) 1928.

with angiomatous changes in the iris and hydrophthalmos. In this case he performed a double trephine operation, with excellent results as to the tension. Microscopic examination of the excised iris showed thickening from proliferation of the endothelial cells, with many newly formed vessels, suggesting an angiomatous condition similar to that found in nevus of the skin. Toward the surface in some places the cells were crowded together in layers, forming nodular protuberances.

Fig. 4.—Roentgenogram, lateral view, showing outline of the vascular growth. The wavy calcified lines show calcified vessels.

He thought that these changes in the periphery obstructed the filtration angle and offered an explanation of the glaucomatous process.

Up to 1927, fourteen cases had been reported, ten of which were in patients with hydrophthalmos. In 1931, Dr. Walter Jahnke[4] of Berlin published a case in which he enucleated an eye for absolute glaucoma associated with nevus flammeus, and in which he found a flat hem-

4. Jahnke, W.: Ztschr. f. Augenh. **72**:354, 1930.

angioma of the choroid with secondary adhesions in the angle of the anterior chamber, which he thought probably caused the increase in severity of the glaucoma. He also found a tortuous network of the diploic veins of the skull. There is no doubt but that congenital nevi are due to some developmental defect in the capillaries of the part affected, and that the increase in the intra-ocular tension in these cases is due to an interference with the excretion of the intra-ocular fluids on

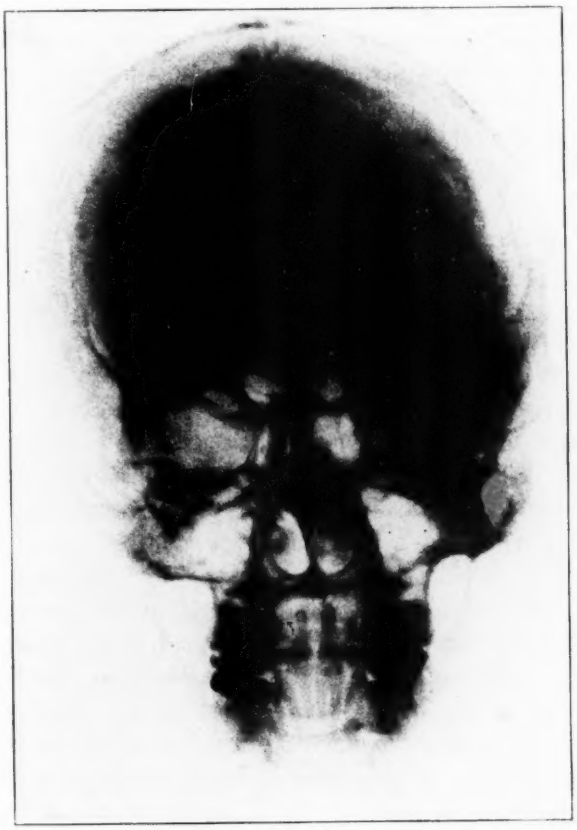

Fig. 5.—Roentgenogram, anteroposterior view, showing outlines of the growth and calcified vessels.

account of chemical changes in the ocular fluids and a blocking of the filtration angle.

These conditions may not manifest themselves for many years after birth, according to Salus,[5] who stated that glaucoma is not always congenital, but may appear as late as the thirty-sixth year. Elschnig,[6] who was one of the first to note the etiologic relationship between nevus and

5. Salus: Klin. Monatsbl. f. Augenh. **73**:305, 1923.
6. Elschnig: Ztschr. f. Augenh. **39**:189, 1918.

glaucoma, thought that the dilatation of the vessels with the associated increase in secretion was the factor producing the ocular hypertension, and he also mentioned that while glaucoma may accompany nevus flammeus, it does not accompany angiomas of the eyelids or face.

Safar [7] found, microscopically, the iris poor in crypts, with no iris ruffle, and he concluded that in his case the glaucoma was due to an interference of the excretory channels of the eye.

While the association of glaucoma with nevus flammeus is rare and interesting, the added and great interest in the case reported consists in the presence of the calcified vascular growth in the left occipital lobe and the wavy lines of calcification extending mesially from the sella to the posterior part of the occipital lobe. According to Cushing and Bailey,[8] the latter condition has been noted in the literature only three times when the growth has been discovered by roentgenography previous to operation. A few have been observed and diagnosed during the operative procedure or an exploratory operation. While in the case reported the right homonymous hemianopia shown in the visual fields was the first sign indicating a possible growth in the brain, it was the roentgenograms as viewed with the skiascopic stereoscope that presented such an extremely interesting picture of the location and nature of the growth that confirmed the tentative diagnosis. While Dr. Boone, the roentgenologist, made a diagnosis of a probable hemangioma, I think, according to Cushing and Bailey's classification, that it is a congenital vascular growth that is losing its vitality and becoming calcified, and that it should be termed a congenital venous angioma of the occipital lobe undergoing calcification. My reasons for placing it under this classification are the negative physical signs, with a normal heart and arteries, and an absence of noises in the head, bruit, choked disks and proptosis. The absence of epileptiform attacks indicates that the lesion is not pressing on the motor area. Cushing and Bailey stated that angiomas are presumably congenital lesions, or at least have some vascular malformation as their basis, and may scarcely deserve to be regarded as tumors, though they may produce irritation or even pressure symptoms indistinguishable from those due to an actual neoplasm. Tumors of the blood vessels are rare; as they are made up of fully formed blood vessels, they are so highly vascular and many of them are aneurysmal or of a cirsoid nature that any attempt at operative removal is unthinkable. Death may occur from spontaneous hemorrhage. In some cases with pressure symptoms, relief has been afforded by decompression. In others, for relief of headaches and pressure symp-

7. Safar: Ztschr. f. Augenh. **51**:301, 1923.

8. Cushing, Harvey, and Bailey, Percival: Tumors Arising from the Blood Vessels of the Brain, Springfield, Ill., Charles C. Thomas, 1928.

toms, ligation of the common carotids and radiotherapy of the vascular growth in the brain have been advocated. In order to add to the literature on these cases, it would be advisable in all cases of nevus flammeus, or nevus trigeminal, to take careful visual fields and to have roentgenograms of the skull taken with the hope of making an early diagnosis and study possible, before pressure symptoms occur to attract attention, and to demand possible operative intervention.

DISCUSSION

DR. MARTIN COHEN: I should like to ask whether the increased vascularity of the uvea, especially of the iris, might not cause increase in intra-ocular fluids and that explain the increase in the intra-ocular pressure.

DR. ARNOLD KNAPP: What treatment is planned in the case of the left eye?

DR. H. H. TYSON: As long as the condition is controlled by miotics, I am going to treat it conservatively, and leave it alone.

DR. MARK J. SCHOENBERG: Dr. Tyson's case reminds me of cases that belong in the same group with those of Lindau's disease.

DR. H. H. TYSON: In reply to Dr. Cohen's question, I think that the increased vascularity with resulting increase in secretion might be considered as a contributing cause.

DR. SCHOENBERG: Is it Dr. Tyson's feeling that the presence of the vascular hypertrophy in the uvea is the main cause of the glaucoma?

DR. TYSON: The hypertrophy seemed to be the cause of the glaucoma in Dr. Knapp's case, and I think that it is also in this case.

GYRATE ATROPHY OF THE CHOROID AND RETINA (FUCHS)

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At a session of the Ophthalmological Society at Heidelberg in 1895, Fuchs [1] discussed an unusual condition of the retina and choroid which he termed retinitis gyrata. At a later period, basing his observations on the study of three cases in Fuchs' private practice, Cutler,[2] at the former's suggestion, wrote at length concerning the changes in the fundus and the general symptomatology of the degenerative process. Soon after the appearance of Cutler's publication, Fuchs observed a fourth case which he, in turn, recorded with his usual degree of accuracy and detail, and the description of which has furnished a background for the few somewhat similar cases that have appeared in the literature since that time.

The case I am about to place on record, while not possessing all of the salient features of those described by Fuchs and others, is so similar in many of its essential details that I have ventured to classify it as Fuchs' gyrate atrophy of the choroid and retina.

REPORT OF A CASE

L. A. T., a boy of 11 years, was referred to me, through the courtesy of Dr. Henry L. Sloan of Charlotte, N. C., in June, 1930. The patient had been under the care of Dr. Sloan since January, 1929, and was seen in consultation by Dr. de Schweinitz about one year later. When first seen by Dr. Sloan, vision, with a myopic correction, was 20/20 in each eye, and subsequent tests showed a slowly progressive myopia and a somewhat reduced visual acuity. When seen by Dr. de Schweinitz, the boy was wearing: O. D. — 1.00 sph. ⌒ — 1.25 cyl. ax. 20 5/9; O. S. —1.00 sph. ⌒ — 1.25 cyl. ax. 180 5/12, and the history was that of an increasing myopia with peripheral retinitis in both eyes. Prior to my examination, the lad, well developed physically and mentally alert, had undergone thorough physical and serologic investigations with negative findings. At 6 years of age he had mastoiditis, which yielded without operation, and he had had most of the usual diseases of childhood. Up to the period when Dr. Sloan was first consulted, the boy's parents were unaware of any serious ocular defect, and were led to seek advice because of reduced visual acuity for distance. Both parents are healthy, are not related and have no ocular trouble. The mother has given birth to three chil-

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Read before the Section on Ophthalmology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 13, 1932.

1. Fuchs, Ernst: Retinitis punctata albescens und Atrophia gyrata chorioideæ et retinæ, Arch. f. Augenh. **32**:111, 1896.

2. Cutler, C. W.: Drei ungewöhnliche Fälle von Retino-Choriodeal-Degeneration, Arch. f. Augenh. **30**:117, 1894-1895.

dren and has had one miscarriage. Two sisters are living and well and free from ocular defects. One aunt, on the maternal side, died of tuberculosis.

After repeated examinations with and without cycloplegics, the following correction was obtained: O. D. — 1.75 sph. ⌒ — 0.75 cyl. ax. 15 20/20 minus; O. S. — 2.00 sph. ⌒ — 1.00 cyl. ax. 180 20/20 minus.

In January, 1931, six months later than the first refraction estimation, the myopia had shown a slight increase, the visual acuity had been reduced to 20/30 in each eye and there was a right hyperphoria of 2 degrees. Both form fields had shown an irregular concentric contraction; the blind spots were slightly enlarged, but no scotomas had been demonstrable in the central fields. The patient recognized colors readily, and up to this period there had been no evidences of night blindness.

Except for a slight prominence of both globes, the external examination gave entirely negative results. The irides were bluish gray, and the pupillary reaction normal to light and accommodation. Slit-lamp findings were negative in both eyes. With the ophthalmoscope, the media throughout were entirely clear. The disks had sharply defined margins and showed no alterations in size, shape or color. The retinal and choroidal vessels were devoid of any pathologic changes. In the midzone of both eyegrounds were numerous fine granular changes somewhat analogous to the condition described as miliary choroiditis, and in the extreme periphery there was a broad zone of irregularly shaped choroidal atrophies forming a complete circle and separated by normal, though deeply pigmented, fundus tissue. The atrophic areas varied greatly in size, shape and distribution. In some instances they appeared as small, round, isolated islands and again as large, irregular areas almost in apposition but separated by thin lines of pigmented tissue. The choroidal vessels coursing over the exposed sclera produced a most striking contrast to the narrow retinal branches which likewise, in many instances, traversed the atrophied areas. Clumps of pigment cells had been deposited here and there on the white fields, but these differed in appearance from those found in retinitis pigmentosa. The striking feature of the affected area was the multiplicity of shapes which the atrophies assumed. Some were irregularly quadrilateral, while others were polygonal. There was no uniformity in the size of the atrophic fields since in many instances extensive areas of the sclera were laid bare and in others the degenerative process had invaded a much smaller portion of the fundus. In all cases the margins, while irregular in contour and frequently lobulated, were sharply defined, and the atrophies appeared as isolated islands surrounded by extremely dark fundus structure. Up to this period the central and peripapillary zones showed no evidences of invasion. In these zones the color of the fundus was of a somewhat darker hue than was normal, and as it shaded off into the affected area the very dark color was even more decided. The broad extraordinary zone in the extreme periphery of both eyegrounds, composed of an unbroken chain of choroidal atrophies of fantastic shapes separated to a greater or less extent by yet uninvaded dark fundus structure and traversed, in most instances, by the broad choroidal vessels and the smaller retinal branches, when viewed as a whole produced the impression of a beautiful mosaic of wonderful design.

While Fuchs regarded this condition as being closely allied to retinitis pigmentosa and retinitis punctata albescens, he felt that the predominance of the choroidal atrophy, which here occupies the foreground of the ophthalmoscopic picture, is ample justification for classifying this degeneration as a separate entity. He belived that while the three diseases have many outstanding symptoms in common, the changes in the

fundus in gyrate atrophy of the choroid and retina are so distinctive that it should be regarded as another degenerative process. The three cases from his clinic, described by Cutler, were in sisters whose ages were, respectively, 21, 24 and 26. The parents were first cousins; the father was dead and the mother had normal eyes. Their symptoms in common were night blindness, posterior polar cataract and a peculiar form of choroidal atrophy at the periphery bounded toward the disk by a lobulated margin of normal fundus. Two of the sisters showed high myopia with marked reduction of visual acuity. In the other the refraction error is not recorded, and vision was reduced to light perception.

In case 1, there was a large staphyloma in the right eye surrounding the disk with peculiar lobulated protrusions extending into normal fundus and farther toward the periphery a uniform zone of atrophy. The edges of the staphyloma and the atrophic zone were sharp in outline and partially marked by pigment. The atrophic area was uniformly white with a few choroidal vessels, and farther toward the periphery it was covered with a dense network of intensely black pigment, so thick that several parts of the periphery were almost black. The left eye showed practically the same changes with some variation in the arrangement of the atrophic areas.

In the second case, described by Cutler, it is evident that the degenerative process had reached the stage where it could be regarded as a true choroideremia. In this instance the whole choroid was atrophied, except for a small area of normal fundus external to the disk. The changes in the fundus, in the case of the third sister, were almost identical to those recorded in the first case, namely, the large staphyloma, the intervening normal fundus and the atrophic zone in the periphery. In this case both disks were slightly atrophied.

Fuchs' fourth case, which he himself reported, was that of a man, aged 29, who came of a healthy family and whose parents were not related. He had suffered from night blindness since childhood, and for several years his vision by day had showed impairment. There was a bilateral myopia of 6 diopters with a visual acuity of 5/36. Both eyes showed practically the same changes in the fundus and both lenses, posterior polar cataract. The retinal vessels were greatly reduced in size, and the disk presented the same appearance as in retinitis pigmentosa. Adjoining the papilla was a large staphyloma, and immediately surrounding this a narrow zone of normal fundus. In the region of the macula only there was an island of normal fundus about the size of the papilla. In a peripheral direction from the narrow normally colored zone was found the atrophic one in which could be observed the individual choroid vessels on the white base of the sclera. Also within this zone were found individual small islands of fundus, normal in appearance and connected by long narrow bridges. The position and form of

Fig. 1.—Section of the affected zone in the case of gyrate atrophy of the choroid and retina.

the islands and the bridges connecting them indicated clearly their method of origin; "it is evident," the author said, "that they are the last remnant of the normal fundus and maintained their position in the midst of atrophic areas." They originated first in the form of roundish spots arranged concentrically in various zones around the papilla, gradually increased in size to such an extent that they almost touched, and finally became flattened so that their outline, which originally had been round,

Fig. 2.—Diagrammatic sketch of the fundus in the case of gyrate atrophy of the choroid and retina, showing distribution of the atrophic areas.

became somewhat polygonal. On the white, atrophic portions of the fundus there were black spots of pigment which were small in the region of the papilla and became larger and larger toward the periphery, where they were large, black as pitch and of plump polygonal form, i. e., different in appearance from those found in retinitis pigmentosa. Fuchs felt that Jacobsohn's case,[3] published in 1888, certainly belonged to this group. In this patient, a youth of 20, the fundus was normal in the

3. Jacobsohn, E.: Klin. Monatsbl. f. Augenh. **26**:202, 1888.

peripapillary and central zones, and the atrophic areas were confined to the periphery. In addition, however, the optic nerve was pale, the retinal vessels constricted and the distribution of pigment rather characteristic of retinitis pigmentosa.

Komoto's case,[4] recorded in 1914, in a young Japanese, was strikingly similar to my own so far as the changes in the fundus were concerned, but differed essentially in that the parents were blood relatives; the child was highly myopic and had suffered from night blindness since early childhood.

The case history described by Bednarski [5] in 1899 was evidently of inflammatory origin secondary to some constitutional disease. He stated that the changes in the fundus were somewhat similar to those described by Fuchs, but as the outstanding feature was a sclerosis of the retinal and choroidal vessels, it is questionable if his case properly belongs to this group.

In a discussion of these cases, Cutler expressed the opinion that the process had run its course and reached a standstill. He said:

> The sharply defined and pigmented edges and the absence of inflammation would point to the stationary character. On the other hand, retinitis pigmentosa is progressive. In thus disassociating the two conditions we weaken the idea of unity which seemed the most plausible explanation, namely, that both the choroidal atrophy and the retinitis pigmentosa are manifestations of the same disease though occurring independently. It is possible that in spite of the stationary appearance of the choroidal atrophy it may still be progressive either in a degenerative way without signs of inflammation or intermittently and in favor of this view must be considered the fact that in all of the cases the essential features of the atrophy were the same. This assumption suggests the possibility of our cases reaching the condition of complete atrophy, which Mauthner's case showed but this is purely an hypothesis.

In a discussion of retinitis pigmentosa and allied diseases, in which is included Fuchs' gyrate atrophy of the choroid and retina, Nettleship,[6] in 1908, thus summarized his views with regard to the part heredity plays in the production of these diseases:

> My principal object has been to appraise the share taken by heredity and consanguinity in causing these maladies and especially to ask whether blood relationship carries any influence at all, apart from the existence of a predisposition to the disease in the two consanguineous parents or ancestors. It is certain that heredity is a potent cause of retinitis pigmentosa and that the descent, though sometimes continuous from generation to generation, either directly from parent to child or

4. Komoto, J.: On So-Called Gyrate Atrophy of the Choroid and Retina, Klin. Monatsbl. f. Augenh. **52**:416, 1914.

5. Bednarski, Adam: On a Case of Atrophia Gyrata Chorioideae et Retinae with Sclerosis of the Choroid, Arch. f. Augenh. **40**:420, 1899.

6. Nettleship, E.: On Retinitis Pigmentosa and Allied Diseases, Roy. London Ophth. Hosp. Rep. **17**:151 and 333, 1907-1908.

indirectly from uncle or aunt to nephew or niece, often shows itself intermittently and may lie hidden for as many as three generations. But of parental consanguinity we cannot at present affirm more than that it often precedes the appearance of the disease; and although we are not yet able to disprove its specific influence, all the direct evidence at our disposal points to marriage of blood relations being harmful only when both husband and wife are members of a tainted stock.

My patient has now been under my observation for two years, during which time his eyes have been studied at frequent intervals. The myopic error has not materially increased, the visual acuity has not been reduced, the form fields show no further contraction and the degenerative process is still limited to the periphery and shows no signs of extension to the central zones. It would therefore seem that in this case the disease may probably be regarded as stationary.

The absence of night blindness, the fact that the parents are not related, and the unaltered appearance of the retinal vessels and disks might well serve to refute the argument that this case should be classified with the group that Fuchs described. But, on the other hand, the broad zone of peculiarly shaped choroidal atrophies, the distribution of clustered pigment cells and the strikingly dark fundus tissue between the white areas correspond so closely with his description of the changes in the fundus that in all essential details they may be regarded as the same picture. In corroboration of this view, I take the liberty of quoting a letter from Dr. de Schweinitz to Dr. Sloan concerning this patient:

> The eyeground is a very interesting one, and the extraordinary zone of atrophy in the periphery, together with the miliary changes in the remaining portion of the fundus, I think indicate that this case should be classified with those to which Fuchs has given the name gyrate atrophy of the choroid and retina. It sometimes remains peripheral and the whole fundus is sometimes involved in the so-called choroideremia. It is true that the lesions are not exactly like those which Fuchs depicted and in most of his cases there was night-blindness, and the affected children were those of consanguineous marriages. Now your patient has no night-blindness, in point of fact he has rather good light-sense as far as it was possible to test this with photo-metric types, and his parents are not related; and yet I hardly know how else to classify this unusual fundus appearance.

Whether or not the case as presented, which lacks some of the cardinal symptoms included in the group reported by Fuchs and others, should be regarded as an unusual form of choroidal atrophy or as a beginning degenerative process which in later life may assume more typically characteristic changes is, as yet, an open question. If, as Fuchs pointed out, the occurrence of atrophy in the form of round constantly enlarging spots suggests the idea that it begins in the center of individual vascular areas and then spreads to their periphery, it is possible that the yet uninvaded central and peripapillary zones of the fundus, in my patient, may later become involved. On the other hand, if Cutler was correct in his hypothesis that the process is a stationary one, the fact that

for over a period of three years there has been no extension of the degenerative process may be significant.

The case is reported because of the striking similarity of the choroidal changes to those which Fuchs described.

ABSTRACT OF DISCUSSION

Dr. T. B. Holloway, Philadelphia: The clinical condition under discussion, originally described by Fuchs and Cutler, has been observed in but few cases, and the group has been included by Nettleship with certain other probably allied conditions such as retinitis pigmentosa, retinitis pigmentosa sine pigmento, retinitis punctata albescens, congenital night blindness and choroideremia. One might with probable propriety refer to the whole group as retinal degeneration, using a qualifying term to indicate the type. But this fact and the presence of certain clinical appearances in the fundus do not necessarily mean that the underlying pathologic process is the same.

As to frequency, the type most commonly seen, retinitis pigmentosa, is rather infrequently observed, and is possibly more apt to be seen in groups in schools for the blind or for deaf-mutes. Further, the borderlines between some of these conditions are none too well defined, and certain cases have been recorded which it was necessary to regard as atypical of the type to which they were assigned. The gyrate type is one of the rarest; to the best of my knowledge no pathologic study has been made in a case of this character, and even in retinitis pigmentosa only a few such examinations are available. The most recent observation by Verhoeff in 1930, and the important experimental observations of J. Friedenwald concerning this condition, will be placed before the section.

After looking over the data recorded in the various case reports of the gyrate type, I find the following characteristics: The condition is not sex limited and is usually seen in the second and third decades, the youngest patient recorded being aged 11 years (McGuire), and the oldest, aged 29 (Fuchs), unless one accepts Mauthner's case, when the age limit would be extended to 32 years. There may be other members of the family with ocular diseases that belong in this large group of conditions. Consanguinity may or may not be present. Night blindness has existed in all except McGuire's patient. Changes of the lens are usually present, most frequently in the posterior part of the lens; in Wernicke's patient they were in the anterior part, and no changes were recorded in Komoto's and McGuire's cases. The vision is much reduced and the fields concentrically contracted, usually markedly so. Myopia has been consistently present in all cases, varying from —1.75 diopters (McGuire) to —20 diopters (Cutler).

More or less atrophy of the disk may be present (none in McGuire's), and this structure is frequently surrounded by an area of choroidal atrophy, but this did not exist in the recorder's case. The earliest signs of the atrophic choroidal areas are doubtless peripheral, but at times they occupy the midzone, while peripheral pigment-clumping and diffuse stippling occur.

Wernicke has expressed the opinion that the changes observed in this condition may be divided into three stages. In the first stage the peripheral atrophic areas slowly fuse and peripapillitic atrophy may develop simultaneously. When myopia exists these changes will usually be regarded as dependent on that condition. He includes in the second stage the fundus changes cited in all the cases then recorded (1909), and personally I may add those in his case and the changes recorded in Komoto's case. Wernicke's third stage had not been seen in any case up to the

time he wrote, although after the extraction of a cataract from his own patient's eye the most advanced changes were observed. In this stage practically all of the normal fundus structures disappear and there is considerable peripheral pigmentation. It may be referred to here that he does not believe this pigment to be stationary, but thinks that it slowly pushes toward the disk. Now, while I have never observed one of these cases, practically all of the case reports are illustrated, and my own views coincide rather closely with those of Wernicke. As a consequence, I believe McGuire's case is the earliest manifestation of this condition on record and is the first that I am aware of to be included in Wernicke's first stage. The factors that might be regarded as against this opinion are the absence of night blindness, consanguinity and the normal disks. As to the first of these, it is well known that even in retinitis pigmentosa it may be concealed, unnoticed, or absent. Consanguinity, while sometimes present, is not consistently so either in this large group of allied conditions or in Leber's disease. In a stage supposedly as early as that in McGuire's case, optic atrophy might well be absent, for, contrary to an opinion that is still too widely prevalent, optic atrophy may be absent in retinitis pigmentosa, as has been shown by pathologic examination and as I have seen clinically in a number of cases.

Since Fuchs' observations, nearly all of the recorders have accepted his views as to the onset of this condition, that is, that the atrophy was primarily choroidal and proceeded from the finer ramifications of the small choroidal vessels. Komoto refers to the atrophy at times associated with myopia but believes that in this condition, as in retinitis pigmentosa, there is a congenital anlage present. He likewise regards the retinal neuro-epithelium as probably first affected, but atrophy of the choroid may go on simultaneously.

It is interesting to note that Mauthner's case is referred to in the literature as the first case of choroideremia and likewise as the first case of gyrate atrophy of the choroid and retina. This would naturally cause one to refer to Parker's (1931) recent tabulation of the recorded cases of choroideremia. The age was stated in fourteen of the fifteen cases recorded, the average age being 27.8 years, while in the nine cases of gyrate atrophy it was 22.3 years. As to sex, all of the cases of choroideremia, except one, were in males, while of the cases of gyrate atrophy, six were in males and three in females. In three of the cases of choroideremia the refraction was not stated, but in the twelve remaining cases it was myopic, varying from 1 to 16 diopters. Myopia was present in all the cases of gyrate atrophy. In other words, in these two conditions the refraction was mentioned in twenty-one of the twenty-four cases, and myopia was present in 100 per cent. I am aware of the assigned etiology of choroideremia, but no pathologic examinations have been made.

Would it be possible to mistake typical gyrate manifestations, if such exist, for the late stages of choroideremia? What is the relation of the myopia to cause and effect in these cases? Time does not permit an adequate discussion of these points.

Now just a word concerning certain cases regarded as atypical, or what Hutchinson thought might be designated as the "mongrel" type. These cases show varying amounts of pigment-heaping associated with a certain amount of atrophy that is usually of the superficial rather than the deeper stromal type. More or less definite sclerosis of the choroidal vessels is apparent. Such a case was described by me in 1914, at which time I referred to Levinsohn's case. Hansell has described a similar one. While Bednarski recorded his findings under the title of a "Case of Gyrate Atrophy of the Choroid and Retina with Sclerosis of the Choroid," subsequent recorders have almost consistently excluded it from the cases of the gyrate type.

VERNAL CONJUNCTIVITIS

OBSERVATIONS ON EIGHTY-SEVEN CASES AT THE WILLS HOSPITAL (1929-1931)

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The medical literature is replete with theories as to the etiology of vernal conjunctivitis. Jacobs,[1] in a recent and excellent review of the present trend of thought regarding this disease, stated that "in view of the present lack of knowledge concerning the etiology of this condition, one would hesitate to use therapeutic measures whose efficacy is still unproven."

Three theories have attracted particular attention:

1. An expression of some constitutional disorder, as of the ductless glands.
2. An evidence of a vagotonic state and lessened suprarenal activity.
3. An ocular manifestation of an allergy.

In the effort to bring about a clearer understanding of this disease, I have paid particular attention to the clinical manifestations, the character, the varieties and the course of this disorder since 1924, during which time I have seen in private and public practice approximately 125 cases.

I am reporting observations on eighty-seven cases, in which careful records have been made at the Wills Hospital during the years 1929, 1930 and 1931. One of the most outstanding conclusions is the fact that a large number of cases of vernal conjunctivitis are unrecognized, because observers in the past have regarded only the cobblestone or pavement epithelium of the lids as the diagnostic feature of the disease, while many cases of the limbic form have escaped attention or have been regarded as phlyctenular conjunctivitis, and a large number of mild follicular forms have been regarded as simple follicular conjunctivitis.

Before one can theorize on the etiology, the diagnosis of the disease must first be agreed on. Certainly the disease is much more prevalent than hospital records indicate. The eighty-seven patients referred to

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From the Clinics of the Wills Hospital.

Read before the Section on Ophthalmology, College of Physicians of Philadelphia, March 17, 1932.

1. Jacobs, M. W.: Am. J. Ophth. **14**:640 (July) 1931.

me from the clinics of the Wills Hospital represent only a fraction of the total number treated in the seven clinics of that institution.

The first and most important conclusion resulting from this clinical study is that vernal conjunctivitis may be two separate and distinct diseases instead of one, caused by the same excitants, just as eczema and urticaria are different diseases. This theory is prompted by the following facts:

1. Not a single case of limbic vernal conjunctivitis was accompanied by pathologic changes of the lids characteristic of the cobblestone lid type.

2. Colored persons manifest only the limbic variety.

3. The pathologic changes in the chronic lid types may persist throughout the winter months, while the limbic form always disappears in the fall of the year.

4. Eosinophilia is highest in the limbic form.

DESCRIPTION OF DISEASE

My observations lead me to describe the disease as follows: It is most likely an ocular manifestation of an allergy, due principally to street dusts, animal dusts and pollens, its onset occurring only in the spring or early summer months, characterized always by itching, by redness of the eyes, most often by lacrimation and by a lardaceous discharge, frequently containing eosinphils, and having the gross pathologic appearance of hyperplasia of the follicles, always of the conjunctiva of the upper lid, rarely of the lower, or it may manifest itself as a vesicular eruption discrete or confluent at the limbus, always involving both eyes, but not necessarily simultaneously.

Its onset as noted in Philadelphia is always from April or May to August, never beginning in the fall or winter months, but once it has developed in the spring or summer, the pathologic changes may be carried throughout the year in the lid type only, and never in the limbic type. The symptoms, itching, lacrimation and discharge of mucus may persist in the winter in the lid type only, but they are trivial and never approach the type of distress found in the hot summer months. The limbic type always disappears completely, both symptomatically and pathologically, with the approach of cold weather and is never seen during the fall and winter months.

Of the eighty-seven cases studied, sixty-two, or 72 per cent, were among male and twenty-five, or 28 per cent, among female patients. This compares favorably with Posey's [2] report of 85 per cent male and 15 per cent female patients.

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2. Posey, W. C.: Tr. M. Soc., Pennsylvania, Oct. 2, 1923; Vernal Conjunctivitis, Atlantic M. J. **27**:215, 1924.

Forty-six cases, or 53 per cent, were of the lid type, and forty-one, or 47 per cent, were corneal or limbic.

Thirty-nine per cent were in the age group 10 years and under (only six patients were under 5); 22 per cent, from 11 to 20 years; 12 per cent, from 21 to 30 years, and 6 per cent, from 31 to 40 years. There were two patients in the group from 41 to 50, and one patient was 59 years of age. These age groups correspond in a measure to those among patients with other allergies.

In conjunctival smears from sixty-nine cases, forty revealed eosinophils; twenty-six of these were of lid type and fourteen of the limbic type; the highest count was 49 per cent in a case of the lid type.

Blood counts were performed in seventy-two cases. Thirty-one revealed an eosinophilia over 4 per cent, the highest count being 21 per cent in a case of the limbic type. Fifteen were of the lid and sixteen of the limbic type.

The duration of the disease is at least two seasons, the average being three years, but many cases last from five to ten years, rarely longer. My oldest patient in the present series was 59 and had had seasonal attacks since early childhood. The youngest patient in this series was 2 years of age (one in private practice was 1 year old—limbic form). Posey mentioned cases lasting twenty-one and twenty-four years; one reported by Saemisch lasted twenty-three years.

CHARACTERISTICS OF LIMBIC AND LID TYPES

The limbic type may last the entire summer. It is never so troublesome as the lid form and has a smaller number of periodic recurrences. Most cases of the limbic type occur in children. Not one case of the limbic type persisted for more than six seasons. The limbic form leaves no telltale pathologic changes. It has been stated by others that a white arcus remains, but many children who have never had vernal conjunctivitis present a scleral epaulet at the limbus. The palpebral type, however, over a period of years, may produce the typical cobblestone with a milky film appearance, will show definite signs of pathologic changes during the winter months and will persistently show the presence of eosinophils in smears during the periods of exacerbation in the spring and summer. The limbic form and the early follicular form, however, show eosinophils less frequently. This accounts in part for the fact that many cases of vernal conjunctivitis do not always reveal the presence of eosinophils.

Keeping in mind the pathology of the advanced stage of the palpebral form, one can readily understand why this type has considerable discharge during the seasonal attack and why the discharge may continue during the winter months in a milder form. The presence of

newly formed tubular glands with newly formed blood vessels containing a single layer of epithelium makes it easy to explain the presence of mucus, white cells and, particularly, eosinophils. Transudation of cells through a blood vessel containing a single layer of cells is quite possible. The newly formed tubular glands become recesses for bacteria. The extraneous matters entering the eye become mechanical irritants and add to the production of more fibrous tissue, more granulations, more mucus and a persistency of the pathologic changes during the winter months. Undoubtedly, bacteria find lodging places in the new crypts, and in this way a secondary bacterial allergy may develop. In like manner, patients with bronchial asthma may become infected with a complicating organism and thus a secondary form of allergy due to bacteria may be produced.

In the limbic type, however, gelatinous swellings about the cornea do not break down and do not ulcerate. Only one case in this series was complicated by ulcer of the cornea. The swellings recede just as do the wheals in urticaria, except much more slowly. In the limbic form, the blood vessels at the limbus become distinct and engorged, and may at times permit the passage of white blood corpuscles, especially eosinophils, through their walls. There is no large amount of secretion compared with the lid type, because no new glands or granulations are formed and no crypts or spongy tissue exists, which might permit the inclusion of extraneous matter or bacteria.

THE LIMBIC VARIETY

The limbic type involves both eyes, there being a single case in this series in which one eye alone showed definite pathologic changes, although itching occurred in both eyes. Single discrete vesicles, one, two, three or more, occur about the limbus. Crops of vesicles side by side may become confluent principally at the upper rim of the limbus, forming a crescent epaulet or gray frosting much like a dense arcus senilis. The lesions are elevated, and there is no healthy cornea between the outermost edge of the limbus and the dirty white, ragged vaccinia-like swelling. Occasionally there may be seen a complete ring of gray swelling at the corneal limbus. The ring band is rarely more than 3 mm. at its widest point. No case in this series had an extensive involvement of the cornea resembling pannus, as reported by other observers. No cases of corneal dystrophy were observed such as was reported by Beigelman.[3]

One crop of vesicles may recede, and others may form at another part of the limbus. The older, disappearing elevations and the fresh,

3. Beigelman, M. N.: Dystrophy of Corneal Epithelium in Vernal Catarrh, Am. J. Ophth. **15**:95 (Feb.) 1932.

newly formed blebs may be in different parts of the same eye, or the old and the new may be side by side. The serial eruptions occur only in the early weeks of the disease, reaching their height of development from three to four weeks after the onset. In other instances the original vesicles or phlyctenules remain the same in number, size and shape until the disease recedes. On incision, the gray area of hypertrophy bleeds scantily, and on staining, this bloody serum shows red cells and white corpuscles, many of which are eosinophils.

The limbic form may be associated with intense itching, but most cases are mild, many patients testifying that very little itching occurs even though the limbic involvement is still extensively present. In other words, the extensiveness of the corneal involvement is no guide to the intensity of the itching. Patients with one or two phlyctenule-like elevations may have very intense itching, while the complete ring involvements may be attended by redness and lacrimation and very little itching.

Dr. Wilmer, in a communication to me, stated that he has had a large experience with vernal conjunctivitis in people from the far South, especially Negroes. "It is interesting that we find such marked involvement of the limbus of the cornea with pigmentation in the Negro."

This corroborates, in a measure, the findings here in Philadelphia of the limbic type in Negroes. This fact also causes me to describe the limbic and the lid type as two separate and distinct forms.

Visual acuity is not materially affected during or after limbic involvement.

PALPEBRAL FORMS OF VERNAL CONJUNCTIVITIS

These forms are simple follicular, cobblestone and giant granuloma.

Simple Follicular Type.—The simple follicular type does not have any typical identifying pathologic characteristics. An intense hyperemia of the conjunctiva of the upper lids, lower lids and bulbar conjunctiva and caruncles are present. Lacrimation accompanies the "bloodshot" eyes. There may be no discharge of mucus, but if a discharge is present, it is scanty. The corneas are clear, and the sight is unaffected except momentarily by the occasional lacrimation accompanying attacks of itching which last from a few minutes to several hours. The most prominent complaints are itching and redness. Of course, the itching is attended by rubbing, and the latter intensifies the redness. The "bloodshot" appearance may precede the severe itching. The so-called milky film does not appear at the onset of the disease, but develops only after two or more seasonal attacks.

The simple follicular form may in some instances be attended by mild itching, so slight as to make the patient regard the disorder lightly and thus fail to apply for medical attention until the second or third

seasonal attack. It is common experience to obtain a history of attacks for several seasons, the patient failing to pay any attention to the ocular disorder until alarmed by the persistency of the periodic attacks. There are instances, however, in which the itching is so intense at the height of the first attack, especially if the summer is very hot and humid, that relief is sought at once. The pathologic changes may remain the same from one season to the other, never reaching the cobblestone stage.

The simple follicular type may last a single season or may recur several summers.

Cobblestone Type.—The cobblestone or pavement epithelium type is described in textbooks on ophthalmology as the characteristic finding of the disease. When this type is seen, it is the advanced stage of the disease after two or more years of seasonal attacks. The pavement epithelium is never seen during the first spring or summer of the disease. The so-called milky film regarded in the past as characteristic is never seen during the first attack, and accompanies most often the cobblestone variety, appearing on the upper and lower lids. It is due to hyaline degeneration just below the conjunctival epithelium. The limbic type never has the blue gray film on the palpebral conjunctiva.

In this group may be classed also the large follicular type which has not yet advanced to the pavement variety. The follicles resemble in every respect those of trachoma, being globular, discrete or clumped, always beginning as a single follicle, but when growth proceeds, pressure from contact fuses them into conglomerate masses or single large granulomas. Single, discrete, hard, partly red, partly pale granules like seeds, two, three or many more in number, may be seen on the upper lids. The tarsal border of the inverted lid may appear as a hair comb, some follicles being fine, others coarse, the nasal half being the fine end of the comb, while the outer half has the coarse teeth. The bulbar conjunctiva is always injected, and the vessel loops of the limbus become prominent, giving the false impression that the limbic type is also present.

When the follicles become flat and broad, the deep fissures between them become quite manifest.

The cobblestones are seen only in the upper lids; the follicles always appear smaller in the lower lids and never assume the flat plateau arrangement of those in the upper lids.

The Discharge in the Advanced Lid Type.—In no ocular disease is the discharge so characteristic or specifically diagnostic as in the advanced lid type of vernal conjunctivitis. The thick, ropy, lardaceous discharge may be peeled off without any bleeding from the conjunctival surface of the upper lid. By massage of the closed lid, it may be dis-

placed to the inner canthus, when it may be removed in one lump by a cotton-tipped applicator, one part attached to the applicator, the other adhering to the lid or inner canthus. It will stretch like chewing gum, and can be rolled *en masse* on the twisting applicator. I have described it as lardaceous, because it looks like a gritty ointment, dirty white, and sometimes an egg shell or cream color. It is thin on the conjunctiva, but when it is gathered by rubbing the lids, it clumps together and forms a good-sized mass, from 2 to 3 mm. in diameter. Several clumped masses may be expressed by rigid massage of the upper lids. Having removed a goodly quantity, added massage may reveal surprisingly more. Very little is stripped from the lower lids.

The discharge contains mucus, epithelial cells, mononuclear leukocytes, eosinophils and polymorphonuclear leukocytes. One would expect a variety of bacteria, merely from contamination by the hands in the act of rubbing, particularly in the case of children, but, curiously, bacteria are few in the smear. I have no doubt that culture would occasionally reveal the common bacteria, but no such study was undertaken on the grounds that this field of research has been covered by others.

The Giant Form.—In this series, there was one case of the giant form of granulations, although I have seen two other patients not under my care. Large, flat granulomas with deep fissures between occupy the entire conjunctival surface of the upper lids. The lower lids have a few small follicles. This type is an exaggerated form of the cobblestone variety. The follicles are large, tough, spongy cushions, the surfaces of which are grayish red, while the borders are rounded and bright red, resembling the fissured tongue of a glossitis. The granulomas on their plateau surface measure from 3 to 8 mm. and are oval, round or quadrate. The discharge is not so voluminous as in the smaller granular type, and, curiously enough, the itching is not so intense.

It should be noted that old cases of palpebral vernal conjunctivitis are always bilateral. The primary attack may be monocular.

ITCHING

The itching also has interesting characteristics. In the lid form, it may be so severe as to cause the patient to remark that he feels like scratching out his eyes. This severity may continue throughout the summer months, receding only occasionally during cold spells in the summer and with the approach of the fall season. The intensity of the itching bears no relation to the grossness of the pathologic lesions. Patients with very few follicles or granulations may have the most severe type of itching, while those with the large granulations complain only slightly.

The itching in the limbic type is never as severe, although it is to be reckoned with in every case.

A most unusual finding is that the itching is most intense at sundown or early evening. I have no explanation for this phenomenon. Little boys will complain of an intensification of the itching after swimming or immediately after playing ball. They may play in the sunlight a greater part of the day without serious annoyance, but the moment they enter the house after the ball game, the itching and redness of the eyes become intense. On humid days, when the weather is sweltering hot, the patients suffer the most. There is no doubt that heat and humidity are not only related to the intensity of itching, but have a direct relation in the production and persistence of the disease.

DIFFERENTIAL DIAGNOSIS

Acute Catarrhal Conjunctivitis.—Vernal conjunctivitis is sometimes confused with acute catarrhal conjunctivitis. In the latter, there is considerable mucopurulent discharge, which when examined microscopically rarely reveals eosinophils, but always one or more types of bacteria and many pus cells. The conjunctiva is uniformly injected, the upper and lower lids being involved alike. The bulbar conjunctiva is deep red, the lids are often swollen, and pain may or may not be present. Itching appears only after the disease has receded, and then it is slight and terminates with the control of the infection. Its period of inflammation is short and never continues two or three months, unless complicated by corneal ulcer or other lesions. It is not seasonal.

"Pink Eye."—"Pink eye" is frequently confused with vernal conjunctivitis; the former disappears rapidly under the usual treatment. A smear taken from the conjunctival discharge will definitely determine the presence of the offending organism of Koch-Weeks. This infectious conjunctivitis may occur at any time of the year, but is seen most frequently in the spring and summer at the time vernal conjunctivitis occurs. The two diseases may resemble each other at the onset, but a few days of observation show the pink eyes as a rapidly progressive, acute disorder, with a mucopurulent discharge, swelling of the lids and a violent inflammation of the palpebral conjunctiva. Itching is not a characteristic of the latter disease, which runs its course at the maximum of two weeks. Cases of vernal conjunctivitis last throughout the summer months.

Trachoma.—The frequency with which trachoma has been confused with vernal conjunctivitis is quite disturbing. The chronic nature of the two diseases, the similarity of follicles of vernal conjunctivitis with the trachoma bodies and the common exacerbations of these eye disorders make differentiation important.

The following cardinal signs will easily distinguish the two:

Trachoma	*Vernal (Palpebral Chronic Form)*
1. Never attended by itching.	1. Always attended by itching.
2. No eosinophils in discharge.	2. Eosinophils frequently found in palpebral form.
3. Vascular cornea seen by slit-lamp. Old cases always show evidence of previous pannus.	3. Cornea clear. Pannus never occurs.
4. No history of return every spring or summer. Exacerbations any time.	4. Return of symptoms regularly spring and summer.
5. No chewing gum mucus.	5. Typical discharge of mucus.

Authors have confused the limbic type as the pannus of trachoma, but one is quite different from the other. In pannus the blood vessels are seen on the surface of the cornea, extending as far as the summit and occasionally completely covering the cornea. In limbic vernal conjunctivitis, the vascularity is limited to a ring of swelling and never involves the entire cornea, and the enlarged vessels always disappear completely with the subsidence of the seasonal attack. In trachoma, the walls of the blood vessels can always be seen by the slit-lamp, even after the disease is cured. Visual acuity is never impaired in uncomplicated cases of limbic vernal conjunctivitis, while in the pannus of trachoma, the acuity is always somewhat impaired. I have never seen trachoma recur regularly each spring and summer and subside with the approach of cold weather. Once trachoma develops, its pathology and symptomatology remain throughout the year until there is a definite recession. Recurrence has no relation to hot weather. The presence of eosinophils in the smear from the eyes or a general eosinophilia in the blood will clinch the diagnosis of vernal conjunctivitis. My pet phrase is, "No itching—no vernal."

PATHOLOGIC REPORT OF TWO CASES OF LID VERNAL CONJUNCTIVITIS

The first case was reported by Dr. Jefferson H. Clark of the Philadelphia General Hospital.

CASE 1.—The specimens submitted consisted of four small bits of tissue, the largest being 1 mm. in diameter. These were blocked, and sections were cut in one plane and remounted, and other sections were cut at right angles to the original ones.

Microscopic examination showed essentially the same histologic changes in all sections: (1) The epithelium was of irregular thickness and somewhat edematous, showing occasional goblet cells overlying (2) connective tissue stroma of varying density and complexity. Many areas were sclerosed and showed an early hyaline change. This was present not only quite deep in the subepithelial tissue, but also just beneath the epithelium. Other areas consisted of younger fibrous tissue, indicated by larger cells with vesicular nuclei. This fibrous tissue stroma showed

(3) numerous capillaries, clearly defined by a single layer of epithelium, and (4) simple glands scattered throughout and lined by epithelium of varying thickness, resembling that covering the surface. In the lumen of these glands could be found (5) eosinophils. Eosinophils were also present throughout the stroma, but were not as numerous as (6) round cells, both lymphatic and plasma in type, being more numerous in the areas composed of younger fibrous tissue.

Histologically, the specimens resembled tissue that was the seat of a subacute and chronic inflammatory reaction.

CASE 2.—Histologic examination of the tarsus of the right upper eyelid from a case of vernal conjunctivitis presented a more varied picture than previous specimens.

The surface was irregular, being divided into flattened, broad papillae, covered by an epithelium of varying thickness, showing numerous hydropic cells.

The stroma was of irregular density. Some areas were edematous and vascular; others were quite fibrous, with hyaline changes. There was a cellular infiltration varying in type and intensity, mainly lymphocytic and plasma cell, but showing in addition many eosinophils. A few simple glands were present lined by epithelial cells, resembling those covering the surface, many also showing vacuolization. Eosinophils were present in the lumen.

The reaction in the tissue was more chronic than in previous specimens, with a subacute exacerbation of greater intensity.

THE CAUSE OF VERNAL CONJUNCTIVITIS

For a long time it has been suspected that vernal conjunctivitis is an ocular allergy. Reports from various sources (Fort,[4] Townsend[5] and Lehrfeld[6]) indicate positive skin reactions to foods and pollens, but failure to obtain a positive skin reaction in all cases of vernal conjunctivitis and the failure of some investigators to obtain any positive reactions (Thommen[7]) caused the ophthalmologic profession to doubt the allergic etiology of this disease. The systematic study of eighty-seven cases of vernal conjunctivitis, assembled during three years at the Wills Hospital, revealed clinical characteristics and laboratory findings which correspond in a measure to those of other allergies, particularly hay fever and asthma. It was my plan to prove the reason for failure to obtain persistent and continued positive skin reactions in cases of vernal conjunctivitis.

Stock preparations prepared by the commercial houses for testing the skin are of uniform strength. They were prepared only for the scratch method. Realizing that many cases of eczema and urticaria,

4. Fort, A. G.: Vernal Conjunctivitis, J. M. A. Georgia **12**:101, 1923.

5. Townsend, J. F.: Vaccine Treatment of Vernal Conjunctivitis, South. M. J. **16**:555, 1923.

6. Lehrfeld, Louis: Allergic Reactions in Vernal Conjunctivitis, Am. J. Ophth. **8**:368 (May) 1925.

7. Thommen, A. A.: Hay Fever, in Coca, A. F., and others: Asthma and Hay Fever in Theory and Practice, Springfield, Ill., Charles C. Thomas, 1931, pt. 3, p. 727; unpublished observations and experiments.

which are believed to be of allergic origin, do not give positive skin reactions and being informed that the scratch method gives 50 per cent less positive reactions than the intradermal method of testing, I proceeded to study two groups of cases, one by the cutaneous scratch method to convince myself of its inadequacy, and the second group by the intracutaneous method, using extracts of varying strengths.

I further realized that the ophthalmologist was not competent to read the results of these tests. I therefore engaged the services of a technician trained in allergic work to perform the scratch tests. A group of nine patients was referred to an expert allergist for the intracutaneous test. Of the twenty-three patients tested by the scratch method, only three gave positive reactions and four gave questionable reactions; of the nine tested by the intracutaneous method, all were positive to house dust, five to grasses and weeds, three to trees and all to animal dusts.

The inequality in the number of cases in these two groups was due to the fact that the technician was located at the hospital and had more cases available for examination, while the patients of the other group were referred to another hospital, many of whom failed to report for examination as would naturally be expected when patients are referred from one dispensary to another in a different institution. Furthermore, the smaller group referred for intradermal testing was referred to a hospital cilinic intended for the treatment of hay fever and asthma, at the height of the season for prophylactic injections. In the confusion generally encountered in clinics for patients with hay fever and asthma, where patients are receiving hypodermic injections, the parents of little children (vernal conjunctivitis most often in children) took fright at the method of diagnosis and treatment and failed to submit to the necessary testing. This, in a large measure, explains the paucity of cases in the latter group.

INTRADERMAL TESTS [8]

The negative reactions are not here recorded.

Joseph S.:

Two grasses—marked.
Ragweed—moderate.
Philadelphia dusts—moderate.
Goose—moderate.
Plantain—moderate.
Chicken—slight plus.
Strawberry—slight.
Blackberry—slight.
Improvement after injection of Philadelphia dusts and two grasses.

8. From reports by Dr. J. Alexander Clarke, Jefferson Hospital.

Stanton H.:

Philadelphia house dusts—slightly moderate.
Orris extract—slightly moderate to moderate.
Goose—slight.
Marked improvement under treatment with orris extract.

James S.:

Dust—moderately marked.
Goose—moderate.
Orris—slight.
Dog—slight plus.
Two grasses—moderately marked.
Cat—slight.
Own dust—marked.
Chicken—marked.
Goose—moderately marked.

Irving A.:

Grasses—slight.
Dusts—moderate.
Chicken—slight plus.

George G.:

Two ragweeds—slight.
Chicken—slight.
Duck—slight.
Cat—slight.
Philadelphia dusts—moderate plus.

Frances S.:

Chicken—slight plus.
Duck—slight plus.
Goose—slight plus to moderate.
Philadelphia dusts—moderate plus.

John S.:

Two ragweeds—moderate minus.
Philadelphia dusts—moderate.
Duck—slight plus.
Goose—slight plus.
Injections of Philadelphia dusts gave marked improvement.

Harry L.:

Two ragweeds—slight.
Two grasses—moderate.
Oak—slight to moderate.
Philadelphia dusts—moderate.
Poplar—moderate.
Walnut—slight.
Chicken—moderate.
Duck—moderate.
Goose—moderate.
Hickory—slight.
Treatment by injections of oak gave some improvement.

Irene H.:

Poplar—slight.
Oak—slight.
Sycamore—slight.
Willow—slight.
Two ragweeds—moderate.
Two grasses—slight to moderate.
Alder—slight.
Philadelphia dusts—marked.
Elm—slight.
Plantain—slight plus.
Sheep sorrel—slight plus.
White ash—slight.
Dog—moderate.
Cat—moderate to marked.
Duck—moderate.
Goose—slight to moderate plus.
Orris—slight to moderate.
Chicken—moderate plus.
Injections of ragweeds, Philadelphia dusts and mixed stock vaccine gave moderate relief.

DETAILED ALLERGIC STUDY OF TWENTY-THREE CASES BY THE SCRATCH METHOD[9]

Physical examinations revealed no obvious endocrine disturbances. Two, or 10 per cent, gave a definite history, and two a questionable history, of other allergic conditions; five, or 21 per cent, gave a definite family history and three a questionable family history of allergy. It is generally conceded that there is an allergic condition in 10 per cent of the population, so that there is in this series a family history of allergy in a larger number of instances.

It seemed desirable to test the patients with all of the foreign proteins, so far as it was possible, with which they came in contact at any season of the year, to determine whether or not they had a hypersensitivity to any which might cause irritation of the eye. These proteins comprised three groups: (1) the pollens present in the air only in spring, summer and early fall, (2) the so-called inhalants, i. e., the animal epidermals and plant substances used frequently in household and particularly bedroom furnishings and dust from the patient's house, and (3) foods. Since vernal conjunctivitis is a condition in which the symptoms recur mainly in the spring and summer, it was felt that patients would more likely be sensitive to the pollens than to proteins. Therefore, each patient, when time permitted, was tested for the pollens and the inhalants at the first visit. In the majority of cases when a positive reaction occurred, the patient was retested for the same substance at some later

9. From a report by Miss Ida Teller, special technician, Wills Hospital.

TABLE 1.—*Results of Tests on Sixteen Patients*

Case	Age	White or Colored	Sex	Duration	Other Allergy				Family History of Asthma	Number of Sensitivity Tests	Number of Tests and Reactions			Eosinophils			Comment
					Asthma	Hay Fever	Eczema	Urticaria			Pollens	Inhalants	Foods	Eye Smear Left	Eye Smear Right	In Blood, per Cent	
1	7	W	M	1930 to Sept. 1931	?	0	0	0	0	8	8 0	.. —	.. —	0 2	0 0	1 2	
2	11	W	F	1929 to Sept. 1931	0	0	0	0	0	17	9 0	8 0	.. —	Innumerable	16 in 20	3	Carious teeth; tonsils enlarged and inflamed
3	2	C	M	1930	0	0	0	0	0	26	10 0	9 0	7 0				
4	7½	W	M	1928 to Sept. 1931	0	0	0	0	0	39	10 0	9 0	19 1?	8 in field of 12		7	Tonsils enlarged and cryptic
5	11	W	M	Jan. 1930 to Sept. 1931	0	0	0	0	0	15	4 0	9 0	2 0	7 in 75	0	6	Dust (2) 0
6	5	C	F	Spring 1930	0	0	0	0	+	24	8 5+	8 0	8 0	0	0	0	"Bronchial trouble"
7	10	C	M	1 month	0	0	0	?	?	31	9 0	10 0	12 0	0	0	6	Dust (2) 0
8	6	W	F	1931	0	0	+	0	?	34	8 0	9 0	17 0	0	8	2	
9	35	W	F	June 1931	0	0	0	0	?	12	5 0 2?	4 0 1?	— —				
10	13	W	M	1928 to Sept. 1931	0	0	0	0	?	37	9 0	10 0	18 0	0	0	0	Excessive sneezing
11	8	W	M	1930 to Sept. 1931	0	0	0	+	+	16	8 0	5 0	3 0	2 in 3	3 in 4	6	
12	8	W	M	1928	0	0	0	0	0	20	10 0 1?	8 0	1 0	..	..	...	Colds and bronchitis
13	25	..	M	1928	0	0	0	0	..	12	4 0	8 0	.. —	3%	0	5	
14	6	W	M	1929	0	0	0	0	+	18	9 0 1?	8 0	.. —	6 per cent		1	
15	59	W	M	1929	0	0	0	0	—	16	9 0	7 0	.. —	0	0	3	
16	14	..	M	1929	0	?	0	0	+	12	5 0 1?	5 0 1?	.. —	0	0	2	

TABLE 2.—*Results of Tests on Seven Patients*

Case	Age	White or Colored	Sex	Duration	Other Allergy: Asthma	Other Allergy: Hay Fever	Other Allergy: Eczema	Other Allergy: Urticaria	Family History of Asthma	Number of Sensitivity Tests	Positive Tests: Pollens	Positive Tests: Inhalants	Positive Tests: Foods	Eosinophils: Eye Smear: Left	Eosinophils: Eye Smear: Right	Eosinophils: In Blood, per Cent	Comment
1	12	W	M	1928 to Sept. 1931	0	0	0	0	..	83	0	0	0	Many	60%	5	Teeth in bad condition; cervical glands enlarged; pulse rapid; temp. 100.6 F.; positive skin reaction to strawberry (13-20) but negative when repeated
2	7	W	M	1929 to Sept. 1931	0	0	0	0	?	61	0	0	0	0	6	2	Teeth carious
3	16	W	M	1929 to Sept. 1931	0	0	0	0	..	67	1?	2?	2?	0	0	6	Tonsillectomy and submucous resection advised; mitral stenosis
4	19	W	M	February 1931	0	0	0	0	+	55	6+	1+	1+, 1 ?	2 to 50		0	Mitral stenosis
5	19	W	F	1931	0	0	0	0	0	76	0	0	2+, 1?	0	0	2	Positive reactions to lamb and egg
6	12	C	M	1930 to Sept. 1931	0	0	0	0	0	76	0	2+	2?	4 to 50		4	
7	21	W	M	1927-28 to Sept. 1931	0	0	0	0	0	86	0	0	6?	6 to 100		1	

Case	Subsequent Tests: Pollens	Subsequent Tests: Inhalants	Subsequent Tests: Foods	Comment
1	0	0	0	Strawberry, 20 mm. erythema at one test
2	0	0	0	
3	1?	2?	2?	Not repeated
4	6+	1+	+	Not repeated
5	0	0	2+, 7?	Reactions, 10 mm. erythema; no check
6	0	2+	2?	Test repeated, +; conjunctiva, positive reaction
7	0	1?	8?	

date. Of the twenty-three patients studied, sixteen did not return to have the tests completed, although on six of them as many as twenty-five or thirty-five tests were done. These sixteen, then, were tested for pollens, inhalants and a few foods. Of these one showed a positive reaction to five different pollens, four showed a questionable reaction to one pollen each, two showed a questionable reaction to a food, and two showed a questionable reaction to an inhalant (table 1).

On the remaining seven patients tests were done with pollens, inhalants and all the foods the patients had eaten more than six times a year. The tests varied in number, ranging from fifty-five in one patient to eighty-three in another. Table 2 gives their reactions.

Of the twenty-three tested, 13 per cent gave positive reactions. Of the seven tested with all necessary proteins, two, or 28 per cent, gave positive reactions.

Results.—Ten per cent of the patients gave a history of other allergic conditions.

Twenty-one per cent gave a family history of allergy.

Of seven patients on whom fifty-five or more tests were done, 28 per cent gave one or more positive reactions.

Of the sixteen patients on whom from eight to thirty-five tests were done (averaging about eighteen per patient), one only gave a positive reaction, but four gave questionable reactions.

The high percentage of positive reactions by the intradermal test, the clinical pictures and blood findings, the periodicity of the disease and the age of incidence point to the allergic origin of vernal conjunctivitis. Until other evidence is presented to prove otherwise, my observations convince me that the cause of this disease is no longer unknown.

REPRODUCTION OF THE CLINICAL SYMPTOMS OF VERNAL CONJUNCTIVITIS

At the suggestion of Dr. Arthur Coca and Dr. J. Alexander Clarke, I introduced the exciting agent into the conjunctival sacs of two patients who had vernal conjunctivitis during the summer months, but who had no clinical symptoms during the winter.

In the first instance, H. L., aged 17 years, was found to be sensitive by the scratch method to June grass, orchard grass, red top and timothy. In the second case, J. S., aged 18 years, was sensitive to June grass, timothy, rye grass, orchard grass and maple. On three different occasions during the month of February, 1931,[10] I instilled these exciting agents into one eye of the respective patients. In case 1, hardly a minute had elapsed before the patient excitedly complained of severe itching in the inoculated eye. Within fifteen minutes, the conjunctiva

10. Demonstrated at the Wills Hospital Clinical Conference.

became intensively injected, red and edematous. Lacrimation became profuse, and the patient became alarmed by the itching. After one hour, a smear was taken of the conjunctival discharge. The laboratory reported the presence of eosinophils. In the second instance, the exciting agents, including maple, were introduced into one eye, permitting the opposite eye to act as a control. Fully twenty minutes elapsed before the redness became apparent, associated with lacrimation and the formation of a thin, ropy discharge, which was found to contain eosinophils. The patient admitted a sense of itching, not very severe. Both patients stated that the irritation of the eye continued for several hours. Four patients who had had vernal conjunctivitis the previous summer, but who gave no positive reactions to the same excitants, were used as controls. The same instillations were made in their eyes in the effort to rule out the fact that the pollen extracts were not in themselves chemical irritants. In all of the control patients, no symptoms developed. There was not even a suggestion of redness. The extract in these cases was that produced by the Arlington Chemical Company.

One would not expect to reproduce in a few minutes the pathology of vernal conjunctivitis which is characteristic only after more than one seasonal attack. Reproducing the clinical signs, namely, redness, lacrimation, itching and local eosinophilia, is sufficient to indicate the specific nature of the two cases here noted.

RADIUM

The reported cures of vernal conjunctivitis by Pancoast, Pendergrass, Laura Lane and myself by the use of radium led me to carry on a study of cases at the Wills Hospital to determine the exact value of this remedy. Apparently convinced of the value of radium as a cure for this disease by the results in two patients treated for me by Dr. Laura Lane in 1924, I became an enthusiastic advocate of the use of radium.

After using this element for three years on twenty patients, under the administration and direction of Dr. B. P. Widmann, radiologist to the Philadelphia General Hospital and the Wills Hospital, his able assistant, Dr. E. W. Spackman, and his technician, Mr. Case, I have conclusively decided that radium is not a cure-all for vernal conjunctivitis, but that it is valuable in alleviating the itching in all forms, and in reducing the pathologic changes in the advanced chronic cases of the cobblestone type.

If vernal conjunctivitis is an ocular form of allergy, it seems unreasonable and unscientific to expect a desensitization of the patient by the application of radium, unless this element can, through the eye, eliminate the patient's sensitivity to foreign proteins. If this were the case, then

one would expect to cure patients with hay fever by applying radium to the mucous membrane of the nose.

One case was sufficient positive proof that radium in itself does not cure. A boy, aged 12, was treated in 1926 by a prominent radiologist for the lid type of vernal conjunctivitis. He was discharged as cured according to the history given by the mother. The summer following, nearly one year after his treatment, his symptoms were so slight that he required no medical treatment. The second summer, however, he had a full return of symptoms, followed again by the third and fourth seasonal attacks. He first came under my observation in the spring of 1930. With his eyes protected by an opaque visor, unable to walk about alone, by reason of the severe sensitivity to light, his head bent and his eyes partly closed, he looked like a patient with frank bilateral interstitial keratitis. Profuse lacrimation and constant rhinorrhea were conspicuous observations.

Physical examination of the eyes revealed the typical lardaceous, dirty white discharge from the lids; the corneas were clear, but the conjunctival surface of the lids resembled that seen in the cicatricial stage of old trachoma. The patient's principal complaint was intense itching and photophobia. The absence of eyelashes in the lower lids and areas of alopecia in the upper lids gave the striking impression of an old trachoma. The itching, however, was so intense and the discharge so characteristic of vernal conjunctivitis that there was no doubt about the diagnosis, in spite of the absence of identifying pathologic changes of the lids. The history, however, confirmed the actual diagnosis. There were no follicles to be seen, no milky film and no resemblance to any case of vernal conjunctivitis I had seen before. It was at once evident that the pathology had been altered by the use of radium. In this instance, the patient had been cured of his pathologic changes by radium, there having been no return of the follicles, but all the clinical symptoms reappeared seasonally. Eosinophils were found in the smear of the discharge and a general eosinophilia in the blood. This case alone convinced me of the usefulness of radium in reducing the pathologic state of vernal conjunctivitis and also proved definitely that it was absolutely not rational to expect a cure of the patient's sensitivity.

All the patients treated by radium may be called pathologically cured from the standpoint of the eyelids alone, but judging from the return of patients with the clinical symptoms of the disease, I firmly believe that radium has a limited value, chiefly in alleviating the symptoms and reducing the granulations.

In this series, I am unable to determine the value of radium in the limbic types. These cases run a seasonal course, despite all treatment, although they can be helped for relief from the symptoms. The ocular

pathologic changes disappear between seasons, and never leave any sequela. Cases desensitize themselves in two, three or four seasons, some longer, and I see no reason for the use of radium except to moderate the itching. As this form disappears completely spontaneously, it is impossible to determine in a given case whether the radium was responsible or whether nature decreed that the last summer attack was to be the final attack.

The itching in all forms of vernal conjunctivitis is decidedly relieved by radium. As the distress from this symptom is so great, I think that one is justified in the use of radium for this purpose.

CALCIUM GLUCONATE

As a calcium deficiency has been found to exist in patients sensitive to proteins and calcium administered to such patients relieves symptoms by decreasing the permeability of blood vessels, it occurred to me that the administration of calcium or parathormone (a parathyroid product) would be helpful in vernal conjunctivitis. Parathormone was reserved for future experimentation. Calcium gluconate (Sandow) was given in heaping teaspoonful doses (90 grains [5.95 Gm.] approximately) in orange juice or milk, one-half hour before each meal. Ten patients carried out this treatment during the heated term in 1930. Each and every one returned regularly asking renewal of the "powdered medicine," expressing the belief that marked relief of itching was experienced. It is difficult to arrive at any definite conclusion except from the subjective reports of patients regarding symptomatic relief. No detail testing was done to determine the calcium content of the blood before or after administration. On the advice of Dr. A. Cantarow of the Jefferson Hospital, who has done considerable work on calcium metabolism, such determination would be not only difficult, but unnecessary. The large doses of calcium were suggested by him on the grounds that an excess of calcium would not be taken up by the blood and that it was natural to strike a balance of calcium. Along with other measures of relief, I believe that calcium has limited value in alleviating the ocular symptoms of vernal conjunctivitis.

A SIMPLE AND EFFECTIVE REMEDY FOR RELIEF FROM SYMPTOMS

Patients invariably claim that itching is relieved following the extraction from the eyes of stringy mucus. Patients will intentionally pick at their eyelids until they have removed the stringy discharge which I have frequently described as "chewing gum" mucus. It occurred to me that the treatment should be directed toward easy removal of the mucus discharge. Furthermore, since in my opinion and in the opinion

of other investigators [11] vernal conjunctivitis is an allergy caused by the introduction of dusts to which the patient is sensitive, it would be important in the treatment of this disease to isolate the patient from that dust or, at least, to isolate his eyes from the dust, and if this is impossible, to bathe the eyes frequently and thoroughly in order to wash out the exciting agents entering the eyes during the course of the day. It is impossible to isolate the patient from the dust except during short periods in the summer months by attending specially cooled moving picture houses where the air is cool and filtered.

The next best plan is to have the patient wear glasses, lightly tinted, to avoid glare and to cut down the intensity of light, and primarily to act as a wind shield for the eyes. Most certainly all the dust cannot be kept out of the eyes by wearing glasses, but a large proportion can.

As the exciting agents with allergic properties are water soluble, it seems plausible that a watery lotion in sufficient quantity and used frequently would be ample to wash away from both eyes not all but nearly all of the exciting agents that may enter the eyes.

To this end, I use one of the most simple and most common remedies known to ocular therapeutics, namely, boric acid solution.

Patients are instructed to bathe the eyes seven times each day, and the following periods are specified:

1. Before breakfast.
2. Before luncheon.
3. After luncheon.
4. Middle of the afternoon (3:00 p. m.)
5. Before supper.
6. After supper.
7. Before retiring.

An eye-cup filled three-fourths with boric acid solution is held firmly against the eye, moving the head backward and forward and blinking the eye as much as possible. The boric acid solution should be cool.

The seven times method of flushing was primarily selected to insure thoroughness, giving the patient definite instructions. Furthermore, seven is easily remembered, even by children. It gives the patient treatment which must be carried on throughout the whole day, and it prevents the accumulation of the "chewing gum" mucus which exaggerates and intensifies the itching.

Boric acid was chosen as the chemical for solution because of its popularity, its inexpensiveness and the ease with which it is prepared in the household. It may be kept cool by storage in refrigerator.

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11. Kruckmann, E.: Some Communications Over the So Called Vernal Catarrh. Wilmer, W. H., Wilmer Institute, Baltimore, personal communication. Fort (footnote 4). Townsend (footnote 5).

Without exception, all patients who used the "boric acid seven times treatment" as it became popularly known in the clinic of Dr. Burton Chance testified that they had marked relief from the itching. The patients who had the disease for several years remarked that the summer of 1931, although it was the hottest and the longest summer for many years, was attended by the least discomfort.

By way of illustration: The wife of a physician, well known to me, has had vernal conjunctivitis for the past five years. She had been using a preparation of zinc and camphor water which alleviated somewhat the symptoms during the attacks of severe itching, but did not in any way abort the attacks or diminish the duration of the disease.

On informing her that I had made a discovery which would give prompt relief from her itching, I prescribed for her the so-called secret formula which was supplied by me through the druggist and not by prescription. An 8 ounce (236.4 cc.) bottle was ordered.

On completion of this quantity, the patient's husband, a prominent internist, called me by telephone, stating that he would like to have the prescription renewed, requesting that I give him the formula so that he might have it made up by a near-by druggist. Of course, I was reluctant to reveal my formula, making him much more anxious to secure it, since he stated that his wife had the first real relief that summer after its use.

Since the physician was a personal friend, I revealed my secret to him on condition that he would not pass the information along to his wife. Of course, there was great laughter following the revelation of my secret, but he promised to keep the information in the strictest confidence.

His wife continued to use the formula, which gave her complete comfort during the remainder of the summer season.

In thanking me for my services, my patient admitted to me that in addition to using my medicine, she added a little boric acid solution to it, believing the original prescription might be too strong for her eyes.

At the present time, I am experimenting on other lotions that will increase the solubility of the "chewing gum" mucus, and thus increase the charm and effectiveness of this great secret remedy—boric acid.

It should be remembered that it is not the boric acid per se which is effective in the alleviation of symptoms, but the continued flushings which keeps the culdesacs free from the exciting dusts.

This remedy is of great value in the simple form of vernal conjunctivitis, both lid and limbic. The chronic lid forms, however, with the large granulations, which have already been complicated by the invasion of bacteria, will require in the initial treatment the additional use of phenacaine, 4 grains (0.26 Gm.), and epinephrine (1:1,000),

20 mm. to the ounce of distilled water, and used as follows: 3 drops in both eyes, three times a day, with an additional dose in the early evening when the itching is most intense. After boric acid flushings have been used for a week, the phenacaine and epinephrine may be discontinued.

Until some other and more efficient lotion is discovered, I am advocating the free use of boric acid solution.

The patient should be seen frequently by the ophthalmologist for the purpose of assisting in the removal of the "chewing gum" mucus, which is readily cleared away by rolling on a cotton-tipped applicator. The lids may be everted and thoroughly flushed with a Ziegler bulb containing boric acid solution.

CONCLUSIONS

Most assuredly, vernal conjunctivitis exhibits the clinical manifestations of an allergy. The negative skin reactions reported in the past are now giving way to positive ones owing to the improved methods of testing and the use of agents of varied and known strength.

It is well known that urticaria, a clinical skin allergy, may not reveal positive skin reactions, that certain cases of asthma cannot be traced to their cause by skin tests, that ragweed dermatitis may not give positive skin reactions, and that there exists an allergy due to mechanical irritation and to heat that is no part of protein sensitivity.

It is also known that intradermal tests give a higher percentage of positive reactions than the scratch method. Furthermore, it is now known that pollens contain an active principal oil as well as a water-active agent. Heretofore, only water-soluble extracts have been used in skin tests. With the discovery that the oily extract is the cause of eczema and the watery extract the cause of hay fever, there is now a new field for investigation which will give more positive reactions, especially in allergic conditions of the skin.

Since the conjunctiva and cornea are closely allied to the skin, it is anticipated that the new refinement in skin testing will reveal a far greater percentage of positive reactions in vernal conjunctivitis. In other words, negative skin reactions obtained by the present method of testing do not disprove the allergic characteristics of this disease, but merely indicate that this particular type of allergy, like some sensitivities, awaits a more delicate biologic test.

ABSTRACT OF DISCUSSION

Dr. B. P. Widmann (Radiologist, Wills Hospital): Whatever may be the cause of this so-called entity of vernal conjunctivitis, there are voluminous reports in the literature that seem to indicate that gratifying benefits have been obtained with the use of radium. Optimism over these results runs parallel with the good effects of radium for trachoma and tuberculous conjunctivitis.

Some observers have been so enthusiastic about the treatment of vernal conjunctivitis with radium that they hold this procedure as almost specific, particularly for the acute and subacute phases of this condition.

There was evidence to indicate that many of the patients with vernal conjunctivitis in whom there were good results were subject to seasonal recurrences. It was thought by Dr. Lehrfeld that this apparent tendency of only transient effects justified an intensive investigation of a group of patients treated with radium. The radiological department at Wills Hospital prepared to study the question of dosage, tolerance of ocular tissue and final end-results. Technical factors of filtration and methods of applying radium with special reference to establishing a minimum dose, time and frequency of application were considered. Factors of dosage established at the Philadelphia General Hospital on the basis of vast experimental and clinical experiences were accepted as the working basis of treatment.

Desjardins [12] made an exhaustive review of the literature, experimental and clinical, demonstrating the action of roentgen rays and radium on the eye.

He found experimental evidence in animals that showed damaging effects on the tissues as well as developmental anomalies resulting from these rays, but only on the growing eye of young animals before birth or during the first and second months of life. Three months after birth the eyes of cats and rabbits were no longer affected by doses that were tolerated by the skin.

Radiologists have found the tissues of the eye tolerant to extremely large doses of roentgen rays and radium in actual clinical experiences of treating malignant disease about the eyelids and naso-accessory sinuses.

Very large doses may cause a permanent alopecia of the lids, severe conjunctivitis, blepharitis, keratitis and cataract. Desjardins found reports of ocular injury following excessive exposure, but he believes that the number of authentic cases is small and that the relationship between cause and effect has not been substantiated.

The rationale of treatment with radium in vernal catarrh is supported by the good effects of radiation for innumerable inflammatory conditions, i. e., adenopathies, boils, carbuncles, eczema, erysipelas and a manifold variety of cutaneous diseases. The mechanism effecting the good results in these inflammatory tissues is not understood, but much credit is given to the well known fact of a profound leukocytic infiltration resulting from radiation.

Our experience with radium for vernal conjunctivitis at the Wills Hospital is quite in accord with the phenomenal regressions and almost specific effects noted by others. The itching and distress of which these patients complained diminished rapidly, to a complete disappearance of symptoms. The granulation tissues resolved; the conjunctiva frequently remained injected for a period of several weeks in the cases showing marked pathologic changes; return of the conjunctiva to apparent normalcy was rapid in the cases of slight local involvement. The intensity of symptoms and the local pathologic changes were not always proportional.

Twenty patients received treatment with radium at the Wills Hospital. The majority of them showed clinical regressions of the local pathologic changes. Symptomatic comfort to complete relief was common. Practically all of the recurrent cases showed seasonal recurrence of symptoms equal to the distress at the start of treatment. It is significant to note that many of the patients showed

12. Desjardins, A. U.: Action of Roentgen Rays and Radium on the Eye and Ear: Experimental Data and Clinical Radiotherapy, Am. J. Roentgenol. **26**: 787 (Nov.) 1931.

no detectable evidence of local pathologic changes and no vestige of the original character of granulation tissue, but presented symptoms of itchiness and pain, comparable if not worse than the symptoms at the outset of treatment. Only about 30 per cent of the patients with recurrent cases who presented no detectable local pathologic changes were relieved symptomatically with further treatment with radium.

These observations justify the conclusion that while the immediate benefits, (*a*) symptomatic relief and (*b*) pathologic tissue regressions, may be so spontaneous as to suggest a specific factor, symptomatic recurrences should be anticipated in from 75 to 100 per cent of cases (without detectable pathologic changes); subsequent responses to radiation are extremely sluggish. This experience is not unlike the phenomenal effects of radiation in certain types of eczema which subsequently resist radiation when there is an underlying constitutional or occupational cause.

It is potentially hazardous to continue treatment with radium for successive recurrences, particularly because of the risk of obtaining cumulative effects of radium. These cumulative effects occur as a result of a diffuse endarteritis of the fine capillary blood vessels, terminating in a degree of fibrosis and hyalinization that interferes with circulation. Late degenerative changes as a result of such alterations in the tissue may occur within two years and even later. For this reason only, moderate radium treatments were given. Filtration was equivalent to 2 mm. of brass, and a plaque was made so that it would cover the entire surface of the eyelid. The treatments were given in quantities estimated as 25 per cent of a full dose, at weekly intervals for four treatments. A small group of patients was given treatment over a period of six weeks. Recurrent lesions were treated in a similar manner. A small group of patients was treated by inverting the eyelid with the radium plaques immediately in contact with the conjunctiva. While the immediate effects of radiation appeared to be satisfactory, the uniform tendency for recurrence of symptoms indicates that there must be a constitutional factor probably allergic in character.

Dr. J. Alexander Clarke (Chief of Hay Fever and Asthma Clinic, Jefferson Hospital): There is a superficial and tantalizing similarity between hay fever and vernal conjunctivitis. Hay fever is a form of allergy in which treatment is most satisfactory, and if it can be proved that vernal conjunctivitis is also of allergic origin, it might be possible to develop a similar simple and satisfactory treatment.

Allergy is the study of the unusual reaction in contradistinction to the usual reaction. For example, the usual reaction to large doses of quinine is ringing in the ears and deafness. Such a reaction can be produced in any one. Urticaria is an unusual reaction to quinine and occurs only in sensitive persons. In order to prove that vernal conjunctivitis is an allergic, or unusual, reaction to some harmless substance, such as pollen, it is necessary to discover and prove such substances beyond a question of a doubt. At present this cannot be done.

The evidence in favor of vernal conjunctivitis being an allergic phenomenon lies in the similarity to hay fever. Both occur in summer, and both have manifestations in the eyes. Both have positive skin reactions to pollens, and in both other manifestations of allergy, such as asthma and eczema, are not infrequently seen. Eosinophils are present in the typical secretion from each. The evidence against vernal conjunctivitis being an allergy consists first in the absence of family history of vernal conjunctivitis. Dr. Lehrfeld tells me that he has never seen two cases of vernal conjunctivitis in the same family. While both have positive skin reactions, it is necessary to use a solution from a hundred to a thousand times stronger to get a skin reaction in vernal conjunctivitis than is necessary in hay fever. In hay fever the severity of the symptoms is directly with the amount of pollen inhaled.

Symptoms of vernal conjunctivitis, on the other hand, do not follow the pollinating periods, but are influenced more by temperature. A very small number of persons suffering from vernal conjunctivitis have been given hay fever treatment, much larger doses being used. The results seem to be worth continuing.

The pathology of hay fever is an urticarial swelling that can be entirely cleared up in a few minutes by the use of epinephrine, whereas the pathology of vernal conjunctivitis is a persistent granulation. In this respect vernal conjunctivitis seems to be more nearly related to eczema, an allergy characterized by a persistent inflammation. Our methods for treating patients with an allergy have helped little, if at all, in the treatment of eczema.

Such are the arguments in favor of and against considering vernal conjunctivitis as an allergy. They are not sufficient to make an unqualified decision. My own opinion is that vernal conjunctivitis is an allergy of the eczematous type, rather than of the urticaria, hay fever group.

COLOR PHOTOGRAPHY OF THE FUNDUS OCULI

DESCRIPTION OF A NEW METHOD

WILLIAM A. MANN, JR., M.D.

CHICAGO

The fundus camera, as simplified and perfected by Nordensen, has made possible in recent years the accurate depiction of lesions of the fundus oculi through the medium of black and white photographs. The numerous advantages of this correct picturization of the actual pathologic changes, especially as relates to the reporting of cases, the teaching of undergraduate and graduate students in ophthalmology and the careful study of the progress of pathologic changes in special cases, have been admirably advanced by Nordensen,[1] Bedell,[2] Von der Heydt [3] and many others. Photographs certainly have an authority and detailed exactness that cannot be equaled by any written word or free-hand reproduction.

The chief disadvantage of fundus photography in the past has been its necessary limitation to black and white. Color and color differences are so important in the diagnosis and appreciation of choroidal and neuroretinal changes that a safe, satisfactory and economical method of photographing the fundus oculi in its natural colors is an advance highly to be desired. This is especially true for teaching and demonstration purposes. Hand-colored enlargements of fundus photographs have been used with some satisfaction, but their preparation is laborious and requires some artistic skill.

Attempts have been made to produce natural color photographs of the fundus by using Agfa or Lumière color plates. These plates have a starch coating containing minute granules in various colors and are quite satisfactory for ordinary photography. Beautiful and accurate reproductions of external eye diseases may be obtained with them, especially in conjunction with the new Bausch and Lomb anterior segment stereocamera. When applied to the fundus, however, the long exposure necessary with the carbon arc lamp used in the Nordensen camera (from

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1. Nordensen, J. W.: Upsala läkaref. förh. **35**:316, 1930.
2. Bedell, A. J.: Photographs of the Fundus Oculi, Philadelphia, F. A. Davis and Company, 1929.
3. Von der Heydt, R.: Am. J. Ophth. **14**:655 (July) 1931.

thirty to sixty times that required for a black and white photograph) is highly deleterious to the sensitive retina. This method has been used by Nida [4] who obtained results with an exposure of eight seconds. Mattis [5] has made natural color photographs of the fundus in blind eyes, using Agfa plates and an exposure of nine seconds in light and twelve seconds in dark eyes. He found that an exposure of five seconds with the arc lamp on his own retina caused a paracentral scotoma and a photophobia lasting twenty-four hours. His requirements for colored fundus photography are: fresh autochrome plates; a blind eye, or one nearly so; sufficient vision in the other eye to fix, and proper fixation of the head for the duration of the exposure. Lijó Pavia [6] has reported success with the use of Colorfilm (Lumière), a new, faster emulsion, exposure to which he believes will not damage the retina. He has found, however, that it is not possible to make satisfactory reproductions from the original plate. He had formerly used Lumière plates with the yellow filter, which required an exposure of from six to ten seconds. The amount of exposure necessary with the new emulsion was not given.

Wessely [7] reported at the International Ophthalmological Congress in 1929 that he had made colored photographs of the fundus by a method involving a different principle from that used in the autochrome plates. A number of exposures were made for various colors with color filters and assembled to form the final colored picture, a process of photography that has had a previous limited use in other branches. It is a rather difficult procedure and very costly.

The method that is here reported is an application of the Finlay natural color process to photography of the fundus. The older type of the Nordensen camera of Zeizz was used because it was the only one available, but the newer reflex-free model should prove just as satisfactory.

METHOD

The pictures are taken through a screen, the emulsion of which is in apposition to the emulsion of the negative. This required having special plateholders made so that both pieces of glass could be made to fit into them in place of the single thickness of glass of the ordinary negative. Any expert mechanic can deepen the old plateholders for this purpose. Use of the Finlay process usually requires about double the normal exposure, but this is obviated by using the new Eastman hypersensitive panchromatic emulsion, which is about twice as fast as the ordinary emulsion of panchromatic plates and which will be made up on order in the 4.5

4. Nida, M.: Concilium ophthalmologicum, 1929, vol. 1, p. 39.

5. Mattis, W. B.: Rev. oto-neuro-oftal. **6**:423 (Oct.) 1931.

6. Lijó Pavia, J.: Rev. oto-neuro-oftal. **6**:427 (Oct.) 1931; Rev. Asoc. méd. argent. **43**:713, 1931; Rev. méd. latino-am. **16**:483 (Jan.) 1931.

7. Wessely, K.: Concilium ophthalmologicum, 1929, vol. 1, p. 44. Wessely and Wertheimer: Klin. Wchnschr. **8**:1624 (Aug. 27) 1929.

by 6 cm. plate size necessary for the Nordensen camera. No practical increase in the ordinary exposure time is thus required. Positives are printed from the negative (after removing the taking screen in the dark room), using glass plates, the ordinary lantern slide plates being quite satisfactory. These appear as black and white transparencies, but on high magnification one can see the fine cross lines produced by the exposure through the taking screen. In front of the dry positive, with the emulsions in contact, is placed the "viewing screen." This must be carefully and painstakingly manipulated with a direct light behind the plate until just the right color values are obtained. While the two plates are held firmly together in the proper position, black lantern slide gummed tape is applied to hold them in correct relationship. The finished picture may be viewed by transmitted light, as in an ordinary viewbox, or by means of a stereopticon lantern, as is true of all types of natural color photographs. Care should be taken to hold the plate perpendicular to the line of vision, as there will be a greenish tint (complementary fundus color) if the photograph is viewed at an oblique angle.

The theory of the Finlay process, as devised by Mr. Clare Finlay, is based on Clerk-Maxwell's theory of splitting the spectrum into three primary colors. The following explanation of how the color is reproduced is given by Mr. Harold Fowler of the New York offices of Finlay Photographic Processes, Ltd.

The taking screen, which is in direct contact with the panchromatic plate and in front of it so that the light passes through the screen before reaching the plate, is really composed of hundreds of thousands of minute tricolor filters. The screen is a regular geometric pattern, 175 dots each way to the inch. These dots are red, green and blue-violet, being exactly the same as tricolor filters.

We will now follow a ray of red light to see what action it has. When the picture is taken, the ray of light goes to the taking screen. Every place where there is a red dot this ray of light will pass through and affect the silver in the panchromatic plate. The red ray will not pass through the green or blue-violet dots; therefore the plate is not affected behind these dots.

When the panchromatic plate is developed, every place where there was a red dot we have a black dot, and where the green and blue-violet dots were we have clear gelatin. From this negative, when dried, a positive transparency is made. This, of course, is just the reverse of the negative. Every place where there was a red dot in the taking screen we now have a white dot, and where there was a green or blue-violet dot we now have a black dot. This positive is now registered with the viewing screen. When the positive and viewing screen are in perfect register, the white dot will go behind the red dot of the viewing screen; the black dots will cover the blue-violet and green dots of the viewing screen. Therefore when the transparency is held to the light, the light will only pass through the white dots of the positive which are behind the red dots of the viewing screen. Therefore we see a red ray of light, the same as that which passed through the camera lens and affected the panchromatic plate.

Combinations of colors are produced by the light passing partly through two of the colors: e. g., violet is produced by light passing partly through the red and the blue-violet but not through the green.

Quite accurate color values are obtained by this method, which may be employed with a little practice by any one proficient in black and

white photography of the fundus. Satisfactory color photographs of the fundus have been made in such typical conditions as medullated nerve fibers of the retina, retinitis pigmentosa, coloboma of the optic nerve, chorioretinitis, coloboma of the choroid and grouped pigmentation of the retina. A number of these were exhibited at the 1932 meeting of the American Medical Association in New Orleans.

SUMMARY

The Finlay process may be used to take natural color photographs of the fundus. The following advantages of this method recommend its use:

1. No increased light or exposure time is required over that necessary for ordinary black and white fundus photography if the hypersensitive panchromatic emulsion (Eastman) is used. This makes the process applicable to all cases suitable for ordinary photography (a dilated pupil and reasonably clear media are essential). All danger of retinal damage is thus eliminated, a factor that has been a deterrent to most previous methods.

2. The method is not expensive, as the taking screens are used over and over and are not damaged if carefully handled. The viewing screens may also be removed from the transparencies and used for others, as desired.

3. As many positives as required may be printed from a single negative. One may make black and white prints from the negative by printing on paper instead of lantern slide plates and omitting the use of the viewing screen.

4. It is possible by means of so-called block-out screens to separate the primary colors in the single negative into three separate positives as a basis for color plates for the printing press. Unfortunately most printers are not as yet familiar with this method of reproduction, but an increased demand could thus be met.

Miss Dorothea Mazanec assisted in much of the technical detail.

RETINITIS PUNCTATA ALBESCENS

REPORT OF TWO CASES IN WHICH THE DOTS DISAPPEARED

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Retinitis punctata albescens was first described by Mooren [1] in 1882. The disease is allied to retinitis pigmentosa, and the name, according to Leber,[2] indicates a type of depigmented tapetoretinal degeneration. Both eyes are affected.

There is often a history of consanguinity in families in which it is found, and several members of the family may be affected, which is significant on account of the rarity of this disease. No instances are reported in which it has been observed in more than one generation in any family. It has been observed rather frequently in families in which retinitis pigmentosa has occurred, although not necessarily in the same generation.

Both sexes are affected and there appears to be no racial predilection, as two cases were reported by Cohen [3] in colored children.

Bell,[4] in describing the condition, stated that night-blindness is almost invariably present from an early age; the retinal arteries may be slightly narrowed, but are never markedly so; the disks may be a little pale, or may be normal; the fields are usually contracted in a dim light and may be so in a good light, and, finally, the visual acuity in a good light may be full or markedly diminished.

Norris and Oliver,[5] on the other hand, stated: "The patients usually suffer from day-blindness . . . the day-blindness has generally existed since childbirth." Later it was added, "Central vision is reduced, while peripheral vision is normal. There is no night-blindness." Nevertheless, in a majority of the cases reported the symptom of night-blindness was recorded. But it seems reasonable to think that with a

1. Mooren, A.: Fünf lustren ophthalmologischer Wirksamkeit, Wiesbaden, J. F. Bergmann, 1882.

2. Leber, T.: Die Krankheiten der Retina: Die sogenannte Retinitis punctata albescens, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, ed. 2, Leipzig, W. Engelmann, 1916, p. 1177.

3. Cohen, M.: Two Cases of Retinitis Punctata Albescens, Arch. Ophth. **45**: 373, 1916.

4. Bell, Julia: Retinitis Pigmentosa and Allied Diseases, in The Treasury of Human Inheritance, University of London, Galton Laboratory, vol. 2, pt. 1, p. 25.

5. Norris and Oliver: System of Diseases of the Eye, Philadelphia, J. B. Lippincott Company, vol. 3, p. 530.

deficiency of pigment the patient might be affected more in bright light and see better in subdued light; at least it was true in the two cases reported in this communication.

Nettleship,[6] who reported the largest number of cases, gave the following description:

> Several conditions have received this title; the name should be restricted to the cases, apparently quite rare, where the fundus is sown pretty evenly with innumerable discrete white dots entirely free from pigment, dull or dead like white paint, affecting the central region as well as or even more than the periphery, apparently dating from birth or early life and remaining, so far as is at present known, stationary; the dots are always small and may be invisible by the indirect method.

There are other conditions in which white dots are seen in the fundus, such as those due to colloid bodies, honeycomb choroiditis or Gunn's ("crick") dots, but Nettleship stated that the condition is so characteristic that once seen it is unmistakable. The dots are deeper than the retinal vessels, which invariably pass in front of them.

Later, in referring to the white dots, Nettleship[7] said that they are:

> Apparently deposits on the choroid or between choroid and retina, separated by comparatively wide spaces of healthy choroid and have every appearance of being minute deposits on, or opaque growths from, the surface of the epithelial pigment layer; these spots are unlike any ordinary spots of retinal or choroidal disease; most of them are round, but some few are oblong or slightly dumb-bell shaped, as if from coalescence of two smaller ones; their size is very uniform, none being wider, and most narrower, than the main retinal vessels; none of them glisten or shine at all, most are entirely free from pigment, but a little black is to be seen at the border of some. . . . In some of the cases there was a good deal of pigmentary collection toward the periphery, but the pigment had not the reticulated pattern of common retinitis pigmentosa.

Leber[2] stated that he believed the dots to be a stronger development and perhaps a partial calcification of the granules of the hyaline membrane of the choroid.

Until there is an anatomic examination, one cannot be sure of the nature of the dots, but it seems possible that small punctate depigmented areas might present somewhat the picture seen and further depigmentation might account for the disappearance of the dots.

Thirty-seven cases of retinitis punctata albescens have been reported in the literature.[8] It seems superfluous to include summaries of them.

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6. Nettleship, E.: A Note on the Progress of Some Cases of Retinitis Pigmentosa Sine Pigmento and of Retinitis Punctata Albescens, Roy. London Ophth. Hosp. Rep. **19**:123, 1914.

7. Nettleship, E.: Cases of Permanent Partial Night-Blindness, with Unusual Ophthalmoscopic Changes, Tr. Ophth. Soc. U. Kingdom **7**: 301,1887.

8. Nettleship (footnotes 6 and 7). Gradle, H.: Further Observations on Retinitis Punctata, J. A. M. A. **49**:301 (July 27) 1907. Ulrich, R.: Typische

The most constant symptom in the cases reported was the white dots. In seven, pigment deposits were described, usually in the periphery of the fundus. Night-blindness was reported in 60 per cent, field defects in less than half of the cases, nystagmus in four, myopia in three and color-blindness or defective color vision in three. Consanguinity and the occurrence of retinitis pigmentosa in the families in which there was retinitis punctata albescens were frequently observed.

In three of the cases reported the dots either diminished in number or disappeared, which indicates the rarity of this occurrence and adds interest to the two cases reported in this communication in which the dots disappeared. Of these three cases Nettleship [6] reported two: In one he observed the entire disappearance of the white dots with the development of several pigment deposits similar to retinitis pigmentosa. In the sister of this patient, who was similarly affected, there was a diminution in the number of white dots. The third case in which the dots disappeared was reported by Gradle;[8a] in this there were associated deposits of pigment in the periphery of the retina. When the patient was seen eight years later, the white dots had disappeared.

The two cases reported here were those of a brother and sister in a family of four children, one girl and three boys. The father and mother were not related, and their eyes were normal except for a small refrac-

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Retinitis pigmentosa mit congenitalen Glaskörper-Anomalien, Klin. Monatsbl. f. Augenh. **21**:140, 1883. Griffith, J.: A Case of So-Called "Retinitis Punctata Albescens," Tr. Ophth. Soc. U. Kingdom **17**:51, 1897. Spengler, E.: Eine ungewöhnliche Aderhautnetz-Hautveränderung auf congenitaler Basis, Ztschr. f. Augenh. **6**:285, 1901. Wuestefeld, F.: Zur Kasuistik der Retinitis punctata albescens, Ztschr. f. Augenh. **5**:110, 1901. Galezowski, J.: Rétinite ponctuée albescente congénitale, Rec. d'opht. **24**:714, 1904. Takayasn, M.: Zur Kasuistik der Retinitis punctata albescens, Arch. f. Ophth. **63**:281, 1906. Van Duyse: Trois cas de rétinite ponctuée albescente typique et familiale, Arch. d'opht. **27**:497, 1907. Healy, J. J.: Retinitis punctata albescens, Brit. J. Ophth. **5**:18, 1921. Lauber, H.: Die sogenannte Retinitis punctata albescens, Klin. Monatsbl. f. Augenh. **48**:133, 1910. Diem, M.: Retinitis punctata albescens et pigmentosa, Klin. Monatsbl. f. Augenh. **53**:371, 1914. Pascheff, C.: Retinitis punctata albescens, Ophth. Rev. **24**:65, 1905. Landesberg, M.: Zur Retinitis punctata albescens, Centralbl. f. prakt. Augenh. **7**:261, 1883. Fuchs, E.: Ueber zwei der Retinitis pigmentosa verwandte Krankheiten (Retinitis punctata albescens und Atrophia gyrata chorioideae et retinae), Arch. f. Augenh. **32**:111, 1896. Agatston, S. A.: Retinitis punctata albescens, Arch. Ophth. **48**:294, 1919. Lievens, E.: Chorio-rétinite albescente ponctuée et pigmentaire, Ann. d'ocul. **158**:829, 1921. Byers, W. G. M.: An Atypical Case of Retinitis Pigmentosa, Am. J. Ophth. **17**:11, 1900. Gayet, A.: D'une lésion congénitale de la rétine est-ce une rétinite pigmentaire? Arch. d'opht. **3**:385, 1883. Scotti, Pietro: A Case of Retinitis Punctata Albescens, Ann. di ottal. **57**:45 (Jan.) 1929. Appleman, L. F.: A Case of Retinitis Punctata Albescens, Arch. Ophth. **2**:377 (Sept.) 1929.

8a. Gradle, H.: Further Observations on Retinitis Punctata, J. A. M. A. **49**:301 (July 27) 1907.

tive error. The other two brothers had normal eyes. Except for color-blindness in a maternal uncle, no allied condition was found or known of in their antecedents.

REPORT OF CASES

CASE 1.—M. W., a girl, aged 18, was first seen on Jan. 31, 1922. She complained of having poor vision and being dazzled by bright light. She also stated that she could see more clearly at night or in subdued light and that she had always been color-blind. She was otherwise well.

Examination of the Eyes.—Vision in each eye was 18/200; with correction, 20/100 in the right eye and 20/200 in the left eye.

There was a horizontal nystagmus of the right eye in the primary position which was not increased in moving the eyes to the right or left. In the left eye there was a slight rotary nystagmus. The patient was totally color-blind. The peripheral fields were slightly contracted.

On ophthalmoscopic examination, the media were clear; the fundi were quite evenly speckled with uniformly small white dots located deeper than the retinal vessels, which appeared to be normal. There were no pigment deposits. The disks had the appearance of the usual myopic disks with small myopic crescents. The fundi were light colored; there was very little pigment, so that the choroidal vessels were distinctly visible, although the patient was a brunette.

There was a compound myopic astigmatism amounting to from 3.50 to 4.00 diopters, which was probably responsible, to some extent, for the poor vision.

The results of a general physical examination and the Wassermann and other tests were reported negative.

When the patient was next seen, about three years later (Nov. 27, 1925), the dots had completely disappeared. The eyes were otherwise about the same, except that possibly there was even less pigment, and the myopia had increased somewhat, although the vision with correction remained the same.

She has been seen from time to time, and at the last examination, on Sept. 4, 1931, there was little change except that the myopia had increased and there were a number of fine punctate opacities in the extreme periphery of both lenses. The fundi were unchanged and there were no pigment deposits.

CASE 2.—A. W., aged 7, a brother of the patient in case 1, was also seen on Jan. 31, 1922. His complaints were the same as his sister's, and he was also color-blind. Otherwise he was well.

Examination of the Eyes.—Vision in each eye was 10/200, and with correction, 19/200. There was also a rather high degree of myopic astigmatism.

There was a horizontal nystagmus in each eye, which was more marked in the right and increased on turning the eyes to the right.

The fundi were almost identical to those of the sister except that possibly there was even less pigment. The patient was also brunette.

He was next seen the same day as the sister (Nov. 27, 1925). The dots had completely disappeared from the fundi; the myopia had increased, but the corrected vision remained the same.

When he was last seen, on Sept. 13, 1930, the ophthalmoscopic findings were unchanged, the myopia had increased a little and vision was the same, but he complained more of being dazzled by bright light.

In 1927, both patients were examined by Drs. F. W. Marlow and S. B. Marlow, who sent me a report of their findings; these were essentially the same as mine. Fields were taken in case 1; the peripheral fields were practically normal, the blind spots were normal and no scotoma was detected with 1.5 mm. test object on the stereocampimeter, even with much reduced light. The light sense, tested with Percival's disks, was also reported normal.

SUMMARY

Retinitis punctata albescens is a comparatively rare disease. The most characteristic and constant sign is the white dots, the nature of which will probably remain a matter of conjecture until an anatomic examination has been made.

Three cases of retinitis punctata albescens have been reported in which the dots disappeared, and to these are added two cases.

THE BIOCHEMISTRY OF THE LENS

I. THE PERMEABILITY OF THE CAPSULE OF THE LENS

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AND
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Satisfactory reviews of the present knowledge of the pathogenesis of cataract are to be found in the monographs of Jess [1] and Siegrist.[2] Salit [3] has recently restudied, with present-day technic, the chemical composition of the normal lens.

THE CHEMICAL CONSTITUTION OF THE LENS

The percentage of the various constituents of the lens varies with age. With increasing years, there is an increase of total protein, lipoid and electrolytes, accompanied by a loss of water and a marked change in the relative amounts of water-soluble and water-insoluble proteins. From the ages of 2 to 16, the protein content of the lenses of cattle rises from 32 to 37 per cent, while the water content falls from 67 to 62 per cent. In new-born calves, the ratio of water-soluble to water-insoluble protein is 80 per cent to 20 per cent; but at 16, the ratio is 41 per cent to 59 per cent.

The water-soluble proteins are the alpha and beta crystallins, which Jess considered albumins, and Woods [4] pseudoglobulins. Woods found that the insoluble protein is a euglobulin, giving immunologically the same reaction as alpha crystallin. From beta crystallin, he has separated an albumin, gamma crystallin, which accounts for the total albumin in the lens (0.2 per cent).

The ether-soluble substances increase from 0.14 per cent in the lenses of calves to 0.63 per cent in the lenses of adult cattle.

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Read before the Section on Ophthalmology at the Eighty-Third Annual Session of the American Medical Association, New Orleans, May 12, 1932.

1. Jess, A., in Schieck, Franz, and Brückner, Arthur: Kurzes Handbuch der Ophthalmologie, Berlin, Julius Springer, vol. 5, p. 170.

2. Siegrist, August: Der graue Alterstar, Berlin, Urban & Schwarzenberg, 1928.

3. Salit, P. W.: Biochemistry of the Aqueous, Lens and Vitreous, Arch. Ophth. **4**:374 (Sept.) 1930.

4. Woods, A. C.: Chemical and Immunologic Researches on Lens Protein, Arch. Ophth. **4**:96 (July) 1930.

There is but 3 per cent ash in the lens; from the first to the seventh decade, a 28 per cent increase of electrolytes takes place, mainly calcium and phosphorus. This increase of electrolytes affects the solubility of the amino-acids and causes a change in their relative concentration: a decrease of cysteine and arginine and an increase of histidine and lysine (Jess).

Recent investigation has demonstrated that cysteine in tissues does not exist free, but is a component of a soluble, thermostabile tripeptide—glutathione (glutamyl cysteinyl glycine). Through the lability of the sulphydryl radical in its cysteine, glutathione is intimately involved in cellular reductions and oxidations. In freshly removed tissues glutathione is mainly in its reduced form. Washed tissues, freed from glutathione, can no longer take up oxygen under aerobic conditions. The normal lens is conspicuously rich in glutathione. In the rabbit, the glutathione content of the lens is 0.33 per cent; of the liver, 0.24 per cent, and of the muscle, 0.04 per cent (Mitchell and Hamilton [5]). Michàil and Vancea [6] estimated the glutathione in various ocular tissues and found the lens to contain 0.356 per cent; the retina, 0.162 per cent; the choroid, 0.078 per cent; the cornea, 0.033 per cent, and the lacrimal gland, 0.05 per cent. Adams [7] found the lens of the ox to contain 0.305 per cent of glutathione, while H. Gifford, Jr.,[8] found 0.34 per cent in the lens of a rabbit.

The equation for the oxidizing and reducing action of glutathione is: $2(\text{SH-glutathione}) + 0 \rightleftarrows \text{S-S glutathione} + \text{H20}$. For oxygen, any other hydrogen acceptor in the tissues can be substituted. The rate of reduction is markedly activated by traces of heavy metals, such as the iron in hemoglobin. Oxidized glutathione is converted back to the reduced form by a thermostabile substance in the tissue. In vitro, lecithin can function as the thermostabile substance. In the lens the thermostabile substance has been identified as beta crystallin. The analysis of lens proteins shows that the glutathione content of the lens is mostly associated with beta crystallin, which Adams also found to contain the thermostabile substance; there is a little glutathione in alpha crystallin, and none in the insoluble euglobulin.

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5. Mitchell, H. H., and Hamilton, T. S.: The Biochemistry of the Amino Acids, New York, The Chemical Catalog Company, 1929, p. 398.

6. Michàil, D., and Vancea, P.: Sur la teneur en glutathion réduit des tissus oculaires normaux, Compt. rend. Soc. de biol. **99**:891, 1928.

7. Adams, D. R.: A Review of the Literature on the Crystalline Lens, Brit. J. Ophth. **9**:281, 1925.

8. Gifford, H., Jr.: Determination of Oxidation-Reduction Mechanism in the Lens of Rabbits with Naphthalene Cataract, Arch. Ophth. **7**:763 (May) 1932.

Tassman and Karr [9] have reviewed most of the available information concerning glutathione and the lens earlier than 1929. The biochemical significance of glutathione in the lens requires much further study. Experimentally, glutathione actively catalyzes the oxidation of fats that contain unsaturated fatty acids. In regard to carbohydrates, the work of Mark [10] indicates that the sulphydryl system is effective only when ferments are present which previously attack the carbohydrate. The relatively low content of glutathione in muscle also suggests that it is not directly related to carbohydrate oxidation. Glutathione may possess a detoxicating action. In vitro, cyanides are oxidized to cyanates, a group only one thirty-second as toxic. Multiplication of cells is favored by glutathione, mainly by stimulating nuclear division in the more mature cells. The cysteine component of glutathione is oxidized to cystine by ultraviolet rays, while the action of infra-red rays in this respect is negligible. This observation, however, seems without significance as an explanation for the genesis of cataract, since experiments on living animals give reverse findings, the lens being markedly affected by infra-red rays and relatively insusceptible to ultraviolet rays. The idea that ultraviolet rays might precipitate lens proteins proposed by Chalupecky was refuted by Jess and Koschella [11] and Lieben and Kronfeld,[12] whose experiments showed that such precipitation occurred only in dilute solutions of the protein, the protein complex in the lens being protected by its high concentration.

The lenses of very young animals, when exposed to cold (15 C. or lower), develop a nuclear opacity that disappears on warming. A similar reversible change occurs when the lenses are placed in hypertonic salt solutions, the opacity clearing on transferring the lenses to physiologic solution of sodium chloride or Ringer's solution. The lenses of somewhat older animals develop perinuclear opacities, but those of adult animals undergo no change. This difference probably depends on the solubility of lens proteins, and definitely indicates a different structure of the central fibers in the young and old.

CHANGES INVOLVED IN THE FORMATION OF CATARACT

The normal human lens tends to become heavier with age through an increase of solids, but with the formation of cataract a gradual

9. Tassman, I. S., and Karr, W. G.: Glutathione in the Crystalline Lens, Arch. Ophth. **2**:431 (Oct.) 1929.

10. Mark, R. E.: Zur Frage der biologischen Sauerstoffüberträgung durch Sulfhydrylgruppen, Biochem. Ztschr. **154**:43, 1924.

11. Jess, A., and Koschella, S.: Ueber den Einfluss des ultravioletten Lichtes auf die Cysteinreakion der Linse, Arch. f. Ophth. **111**:370, 1923.

12. Lieben, F., and Kronfeld, P.: Ueber die Wirkung der Belichtung auf die Eiweisskörper der Augenlinse, Biochem. Ztschr. **197**:136, 1928.

diminution in the weight of the lens occurs; the more mature the cataract, the greater is the loss of weight (Deutschmann, Jess). Kubik,[13] in an extensive study of lenses removed in the capsule, determined that the average weight of lenses with almost mature cortical cataract was 0.209 Gm.; of mature cataracts, 0.188 Gm. Similarly, Clausnizer [14] ascertained that the average weight of dislocated transparent lenses was 0.227 Gm.; of dislocated opaque lenses, 0.183 Gm. In experimental parathyroidectomy cataract, Evans and Kern [14a] found the same loss of weight; whereas the weight of the average normal dog's lens was 0.469 Gm., that of the cataractous lens was 0.4275 Gm. But in spite of this loss of weight, there was a significant increase in the water content, from 61 to 64 per cent. The loss of weight due to loss of solids in the cataractous lens seems of especial significance when contrasted with the increase of weight that occurs in the clear senile lens. Kubik proved that lenses with nuclear sclerosis or cataracta brunescens showed an increase of weight, which suggests that this type of opacity of the lens represents the natural outcome of senile changes, while cortical cataract would seem to depend on some factor that interferes with the normal processes.

The more total the opacity, the more the lens consists of the insoluble, glutathione-free euglobulin. The crystallins disappear (Jess). In the determinations of O'Brien and Myers,[15] the cholesterol increased from 0.4 per cent in the normal lens to 0.51 per cent or 0.7 per cent in the cataractous lens. The blood cholesterol of the patients with cataract was also slightly above normal. Michàil and Vancea [16] produced hypercholesteremia in rabbits by feeding them naphthalene.

Burge [17] discovered in cataractous lenses an increase in calcium and a decrease in potassium. In the cataracts experimentally produced by parathyroidectomy, Evans and Kern found that the calcium rose from 1.2 per cent of ash in the normal dog's lens to 28.7 per cent, and that the potassium fell from 29.5 to 21.8 per cent.

The long period generally involved in the development of opacities indicates the extreme slowness of lens metabolism. In cases in human

13. Kubik, J.: Zur Pathologie menschlicher Stare, Arch. f. Augenh. **102**:657, 1930.

14. Clausnizer, T.: Weitere Ergebnisse von Wägungen der in geschlossener Kapsel entfernten menschlichen Linse, Centralbl. f. prakt. Augenh. **35**:262, 1911.

14a. Evans, E. I., and Kern, R.: Relation of Parathyroid Gland to Cataract, Am. J. Ophth. **14**:1029, 1931.

15. O'Brien, C. S., and Myers, V. C.: Chemical Analyses of Blood in Patients Having Senile Cataract, Arch. Int. Med. **42**:376 (Sept.) 1928.

16. Michàil, D., and Vancea, P.: Der Cholesterinstoffwechsel der Organe im Verlauf der Naphtholinergiftung, Klin. Monatschr. f. Augenh. **82**:844, 1929.

17. Burge, W. E.: Analyses of the Ash of the Normal and the Cataractous Lens, Arch. Ophth. **38**:435, 1909.

beings following lightning or electric shock, the latent period is from six to eighteen months; following parathyroidectomy, from several months to two years, and after overexposure to radium or the x-rays, from two to eight years. Adams found that in hypermature and in old traumatic cataract in human beings both glutathione and the thermostabile reduction system were absent from the lens, while in cataracta brunescens, which represents a pure nuclear sclerosis, glutathione was absent, but the thermostabile substance was still present. She later [18] reported that glutathione was entirely absent from the lens in naphthalene cataract. H. Gifford, Jr.,[8] reviewed the work on naphthalene cataract, and reported that glutathione is present in normal amounts in the early stages and is present in traces in the mature forms. Thus the loss of glutathione would seem to follow rather than to initiate the appearance of opacities. Michàil and Vancea [19] thought that the changes resulting from naphthalene were due to the damage of the islands of Langerhans that they demonstrated in their animals. By giving insulin they were able to retard the development of the opacities of the lens, prevent the development of pigment in the cataractous lens, owing to the oxidation of tyrosine, and even cause this pigment to disappear where it was already present. They seem to have disregarded the marked variability in the formation of cataract due to naphthalene that was observed by H. Gifford, Jr.

The loss of glutathione in the cataractous lens is accompanied by a fall in its respiration. Using the Winterstein respirometer, Mashimo [20] determined that at 30 C. the average consumption of oxygen per hour of the normal lens of the rabbit was 60 c.mm. while that of cataractous lenses was from 3 to 15 c.mm. This was confirmed by Kronfeld [21] and by Schmerl and Thiel.[22]

THE RÔLE OF THE CAPSULE OF THE LENS

The vital importance of the capsule of the lens as the medium of biochemical interchange between the lens fibers and the aqueous has caused some investigators to consider capsular abnormalities as important factors in the genesis of cataract.

18. Adams, D. R.: The Nature of the Ocular Lesions Produced Experimentally by Naphthalene, Brit. J. Ophth. **14**:49, 1930.

19. Michàil, D., and Vancea, P.: L'action de l'insuline sur l'évolution de la cataracte naphthalinique, Compt. rend. Soc. de biol. **96**:65, 1927.

20. Mashimo, M.: Ueber den Gaswechsel der Linse, Klin. Wchnschr. **2**:1809, 1923.

21. Kronfeld, P.: Zur Frage der Linsenatmung, Ber. u. d. Versamml. d. deutsch. ophth. Gesellsch. **46**:230, 1927.

22. Schmerl, E., and Thiel, G.: Ueber des Membranpotential der Linsekapsel und das Auftreten der Natriumnitroprussidreaktion im Kammerwasser, Arch. f. Ophth. **122**:482, 1929.

One of the first modern conceptions of cataract was that expressed by de Quengsy in 1789. This was that a disturbance of the flow of nutrition into the lens by obstruction of its vascular supply took place, resulting in opacity. Becker (1877) held a similar theory of malnutrition which he thought might be due to irregular sclerosis of the lens fibers or to abnormalities in the fluid nourishing the lens. Deutschmann (1879) took the opposite point of view, believing that the lens fibers absorb an abnormal amount of fluid, which causes them to swell and break down, the lens protein passing into the aqueous. He considered as evidence of this the loss in weight of the cataractous lens, as opposed to the increase in weight of the normal senile lens, which he was apparently the first to record accurately.

More recently Löwenstein,[23] basing his conclusions on the occurrence of traumatic cataract following rupture of the capsule of the lens, presented a theory that senile cataract is caused by an increased permeability of the capsule of the lens in old age. This allows the aqueous, and especially certain crystalloids contained in the aqueous, to penetrate the lens, causing cataract. He considered the occurrence of cataract after massage of the lens and after detachment of the zonular lamellae in glass-blower's cataract as evidence in this direction.

Löwenstein first observed that aqueous, either untreated or treated to destroy any lytic ferment present, produced opacity of the lens protein, but in his later work with Haurowitz [24] he found that this depended on other factors and was unable to demonstrate any protective action of the capsule on the lens. Opacities of the lens due to cold, salt or acid were unaffected by the state of the capsule. The clouding of the lens that occurred when the reaction was made from p_H 5 to p_H 6 was due, he found, to precipitation of alpha crystallin, the beta crystallin and euglobulin remaining clear through a range of from p_H 5 to p_H 8.

Schmerl, in estimations of the lens metabolism by the Warburg method, noted a marked increase in the rate of consumption of oxygen when the capsule of the lens was damaged, and interpreted this as due to increased permeability of the capsule. Kronfeld [21] noted a sudden increase in the consumption of oxygen after the rabbit's lens had been in the respirometer for twelve hours, which he considered due to a breaking down of the capsule of the lens.

23. Löwenstein, A.: Eine neue Anschauung über die Entstehung des Alterstars, Arch. f. Ophth. **116**:438, 1926.

24. Löwenstein, A., and Haurowitz, F.: Experimentelle Untersuchungen über das Verhalten der Rinderlinse bei Veränderung des umgebenden Mediums, Arch. f. Ophth. **122**:654, 1929.

Schmerl and Thiel [22] examined lenses of rabbits with naphthalene and roentgen cataracts and those in which the capsule had been damaged by massage. In such lenses a marked increase in the consumption of oxygen was noted, and also a lowering of the membrane potential as compared with that of normal lenses. The aqueous of such eyes was found to give a positive reaction to sodium nitroprusside, whereas the aqueous of normal eyes regularly gave a negative reaction. These findings were interpreted as being due to increased permeability of the capsule of the lens in these conditions. Degenerative changes in the capsule were found in naphthalene cataract by Panico [25] and others, and have been considered the cause of the opacities of the lens that develop.

The characteristic subcapsular location of the opacities in cataracta complicata, irradiation cataract, the cataract occurring in myotonia atrophica and that due to parathyroidectomy and naphthalene is certainly suggestive of a relation between these conditions and changes in the capsule. In certain cases of senile cataract, however, it must be remembered that the opacity does not usually commence beneath the capsule, but in deeper layers of the cortex, as Vogt and Horlacher [26] have shown. Nuclear senile sclerosis leading to cataracta brunescens is probably of a nature different from that of the subcapsular forms. Lo Cascio found no histologic changes in the capsule in this type of cataract, while in cortical cataract certain changes were found. He concluded that no protective action on the lens was exerted by the capsular epithelium (quoted by Scotti [27]).

Scotti repeated the experiments of Hess with ultraviolet rays, and found that in rabbits fairly large doses (over three hours) produced vacuoles in the capsular epithelium but no opacities in the lens itself, much larger doses being required to produce opacities beneath the capsule.

Those who believe that increased capsular permeability is involved in the formation of cataract maintain that this change is to be anticipated from the effect of age on colloidal membranes. Child,[28] however, has shown that the tissues become decreasingly permeable with age, and he considers this decreasing permeability as one of the important factors that lead to senescence. Lasareff [29] and Shastid [30] were of the

25. Panico, E.: Cataratta naftalinica, Ann. di ottal. e clin. ocul. **56**:799, 1928.

26. Vogt and Horlacher, cited by Siegrist (footnote 2).

27. Scotti, P.: Alterazioni del cristallino da raggi ultra-violetti, Ann. di ottal. e clin. ocul. **58**:963, 1930; **59**:19, 1931.

28. Child, C. M.: Senescence and Rejuvenescence from a Biologic Standpoint, Bull. New York Acad. Med. **5**:111, 1929.

29. Lasareff, E. G.: A New Cataract Theory, Russk. j. opht., 1928, p. 710.

30. Shastid, T. H.: Treatment of Incipient Cataract, Am. J. Ophth. **12**:665, 1929.

opinion that pressure contact of the ciliary processes during accommodation has a disintegrating effect on the capsule. They assumed that this damage is particularly prone to occur in advancing age, when the lens is greatly increased in its frontal diameter and the ciliary muscle is stimulated to overactivity by uncorrected or insufficiently corrected presbyopia. The aqueous then slowly penetrates into the lenticular substance, and the formation of a cataract results.

More direct evidence concerning the permeability of the capsule of the lens has been presented by Hess [31] and Friedenwald.[32] The former showed by experiments with dialysis that the normal capsule of the lens is freely permeable to water and electrolytes. Friedenwald, in experiments on the freshly removed capsule of the lens, showed that it is permeable not only to water and electrolytes, but also to dyes of rather high molecular weight. Testing the capsules of beef lenses from animals of different ages, he found definite evidence of decreased rather than increased permeability in the older animals. Additional evidence concerning the permeability of the normal capsule comes from Nicloux and Redslob,[33] who found that alcohol passed freely into the lens when given by mouth, the concentration being half that in the blood after three hours. Daniels [34] was able to detect iodine in cataractous lenses of human beings in amounts of from 0.045 to 0.347 per cent, by bathing the eye in 1 per cent solution of sodium iodide for ten minutes on from two to sixteen successive days prior to extraction.

Since a number of questions concerning the permeability of the capsule of the lens seemed undecided, experiments were conducted to study this permeability in normal lenses, lenses with experimental cataract and cataractous lenses of human beings removed by the intracapsular method. The technic of studying the isolated capsule of the lens seemed somewhat delicate and was open to the objection that the necessary manipulation might damage it so as to change its permeability, although Friedenwald's constant results would indicate that this was not the case. It seemed simpler and more nearly approaching natural conditions to study the lens as a whole, using the capsule as a dialyzing

31. Hess, C.: Pathologie und Therapie des Linsensystems, in Graefe-Saemisch: Handbuch der gesamten Augenheilkunde, ed. 3, Leipzig, Wilhelm Engelmann, 1911, vol. 6, p. 35.

32. Friedenwald, J. S.: Permeability of the Lens Capsule: With Special Reference to the Etiology of Senile Cataract, Arch. Ophth. **3**:182 (Feb.) 1930; The Permeability of the Lens Capsule to Water, Dextrose and Other Sugars, ibid. **4**:350 (Sept.) 1930.

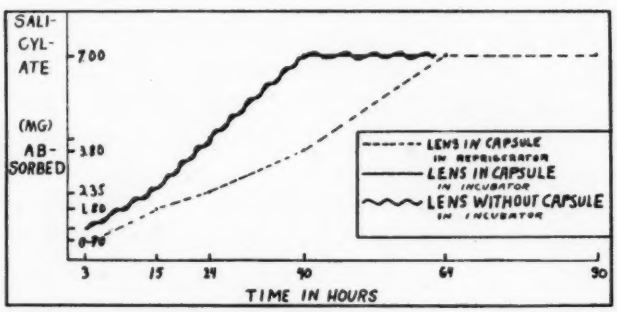
33. Nicloux, M., and Redslob, E.: Passage de l'alcool ingéré dans le corps vitré et le cristallin, Comp. rend. Soc. de biol. **107**:997, 1931.

34. Daniels, B.: Untersuchungen zur Jodbehandlung der Kataracta senilis, Ztschr. f. Augenh. **75**:129, 1931.

membrane. As glutathione, albumin and globulin were present in the lens, they were estimated in the surrounding fluid to determine the permeability of the capsule from within out, while other substances of varying molecular size were added to the fluid and the amounts in the lens after various lengths of time estimated in determining the permeability from without in. These experiments were performed with freshly removed lenses of cattle, sheep, rabbits and dogs. For experiments on the lens in vivo, rabbits were given injections of various substances, and the amount of these substances present in the lenses (after removal of the capsule) was estimated. A few cataractous lenses

TABLE 1.—*Permeability of Lens With and Without the Capsule*

Time, Hrs.	Refrigerator (Lenses with Capsule) Mg. Salicylate Absorbed	With Capsule Mg. Salicylate Absorbed	Without Capsule Mg. Salicylate Absorbed
3	0.70	1.10	1.10
15	1.80	2.50	2.50
24	2.35	4.20	4.20
40	3.80	7.00	7.00
64	7.00	7.00	7.00
90	7.00	....	....



of human beings removed by the intracapsular method were available for experiments with dialysis. In addition, the lenses of rabbits with naphthalene cataract in various stages were used for dialysis to determine whether changes in the permeability of the capsule occurred.

SUMMARY OF EXPERIMENTAL WORK

I. THE INFLUENCE OF THE CAPSULE IN THE ABSORPTION OF SODIUM SALICYLATE; THE INFLUENCE OF TEMPERATURE

Conditions of Experiment.—Fresh beef lenses (average weight 2.2485 Gm.) removed from eyes about one and one-half hours after death were dialyzed in 10 cc. of 0.5 per cent [35] sodium salicylate for

35. Enough of an isotonic solution of sodium salicylate was added to Ringer's solution to make this percentage. In this strength, the salicylate solution is bacteriostatic.

various periods. At the end of these stated periods, the amount of salicylate in the lens was estimated after grinding, acidification and extraction with anhydrous ether. Quantitative determinations were made by the addition of ammonio-ferric alum and comparison with a standard color scale.

Interpretation of Findings.—It is seen that the presence of the capsule of the lens does not affect the absorption of sodium salicylate. In the incubator, absorption proceeds more rapidly than in the icebox, an equilibrium between the lens and the surrounding fluid being reached after forty hours in the first case and sixty-four hours in the latter (table 1).

II. PERMEABILITY OF THE LENS TO SUBSTANCES OF VARYING MOLECULAR SIZE FROM WITHOUT

A. Absorption Through the Capsule.—Condition: Beef lenses were dialyzed in physiologic solution of sodium chloride to which was added sodium salicylate or fluorescein to a concentration of 1:1,000. The amount of the substance present after from two to sixty-eight hours was estimated in series 1 and 2 (table 2). The salicylate was estimated as previously described. The fluorescein was extracted from the crushed decapsulated lens with distilled water and estimated by comparison with a standard color scale in tubes of equal size in the beam of a micro-arc lamp, a Corning G.986 filter being used. Insoluble lens material was removed by high speed centrifugation, and the opalescence of the resulting solution was equalized by the addition of lens extract to the tubes of the color scale. It is possible that in these experiments some salicylate or fluorescein remained unextracted, but since the amount could not be large and would be similar in all groups, the comparative value of the findings was not affected.

As an expression of permeability was used the amount of reagent present in the lens divided by its surface area, which was calculated from the average weight of the type of lens employed (P/A).

Interpretation: The capsule is freely permeable to both sodium salicylate and fluorescein. The permeability to sodium salicylate is greater than to fluorescein during the earlier hours of the experiment. After from eight to twelve hours, the capsule has apparently undergone certain changes, and this is here shown by a greater permeability and by less difference in respect to the reagents of different molecular weight.

In addition to the foregoing determinations, permeability to congo red (molecular weight, 652) and mercurochrome-220 soluble (molecular weight, 804) was estimated for a small number of lenses. Quantitative determinations were not made, but it was found that an appreciable

amount of both reagents was present in the lens substance after dialysis for two hours.

B. Absorption of Sodium Salicylate by Cortex and Nucleus.—Conditions: Beef lenses were dialyzed in 0.5 per cent sodium salicylate, and the amount present in the nucleus alone after varying periods was compared with that in whole lens of a similar weight after the same period. The part of the lens showing definite opacity while in the icebox was taken as an arbitrary measure of what could be considered the nucleus. This was approximately one-third the diameter of the whole lens, and the cortex of the lens was rubbed off to leave a central portion of this size.

TABLE 2.—*Permeability of the Capsule of the Lens for Sodium Salicylate and Fluorescein*

Time in Hours	Average Weight in Gm.	Surface Area in Sq. Cm.	Mg. of Salicylate in the Lens	Ratio of Permeability P/A	Mg. of Fluorescein in the Lens	Ratio of Permeability P/A
			Series 1 at 20 C.			
2	2.2485	7.6913	0.125	0.0162	0.04	0.0052
4	2.2485	7.6913	0.125	0.0162	0.08	0.0104
8	2.2485	7.6913	0.125	0.0162	0.08	0.0104
20	2.2485	7.6913	0.166	0.0216	0.16	0.0211
			Series 2 at 4 C.			
4	2.2485	7.6913	0.066	0.0085	0.040	0.0052
8	2.2485	7.6913	0.083	0.0108	0.055	0.0071
12	2.2485	7.6913	0.125	0.0162	0.080	0.0104
21	2.2485	7.6913	0.240	0.0325	0.100	0.0130
35	2.2485	7.6913	0.300	0.0390	0.160	0.0208
44	2.2485	7.6913	0.400	0.0507	0.207	0.0269
68	2.2485	7.6913	0.500	0.0648	0.400	0.0570

Interpretation: No salicylate could be detected in the nucleus until after forty-eight hours in the refrigerator or twenty-four hours in the incubator (table 3). After one hundred and twenty hours in the refrigerator, the amount in the nucleus was but one twenty-fifth of that in the whole lens in proportion to weight. In the incubator considerable autolysis has occurred by this time, and the proportional amounts in nucleus and cortex are the same. The slow absorption by the nucleus is in line with what we know of the sluggish metabolism in this part of the lens and may be of importance in senile sclerosis of the nucleus.

III. PERMEABILITY OF THE CAPSULE TO SUBSTANCES CONTAINED IN THE LENS

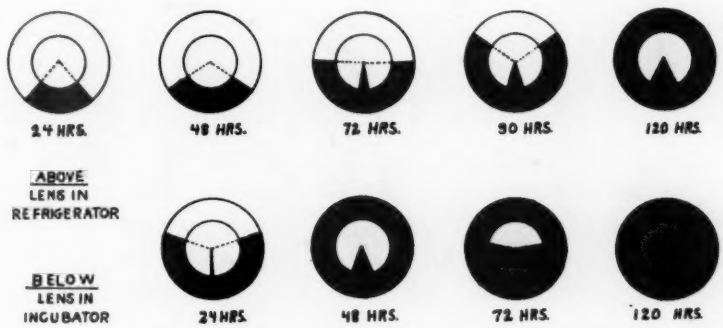
Conditions and Results.—Fresh sheep lenses were placed in tubes containing 5 cc. of Ringer's solution. These were kept at room temperature, and at the end of two, four, six, eight, twelve, fourteen and twenty-one hours the dialysate was removed and examined:

A. The dialysate gave faintly positive reactions for albumin after two hours and sharply positive reactions after eight hours. Tests with nitric acid, thiosalicylic acid and mercuric chloride were utilized.

B. The reaction to sodium nitroprusside was faintly positive after four hours and markedly so after eight hours. The molecular weight of glutathione is relatively small (292), so that the slight amounts found in the early tests probably indicate that only such small amounts

TABLE 3.—*Absorption of Sodium Salicylate by Cortex and Nucleus*

Place	Hours	Weight (Gm.)		Salicylate Absorbed (Mg.)		Ratios	
		Lens	Nucleus	Lens	Nucleus	Weight Nucleus to Weight Lens	Salicylate Absorbed by Nucleus to that Absorbed by Lens
Refrigerator	24	1.8339	0.4383	1.75	....		
	48	2.0200	0.4380	2.50	....		
	72	1.8685	0.4662	4.00	0.10	0.250	0.025
	90	1.8370	0.4965	5.53	0.20	0.270	0.036
	120	2.1430	0.5400	7.87	0.30	0.252	0.038
Incubator....	24	1.8602	0.5200	4.20	Trace		
	48	1.9920	0.4650	7.00	0.25	0.233	0.036
	72	1.9020	0.3900	7.00	0.80	0.205	0.114
	120	2.3430	0.5090	7.00	1.50	0.218	0.214



are freed from combination with the lens protein and are not indicative of an impermeability of the capsule for this substance.

C. Globulin, the molecular weight of which (about 100,000) is greater than that of albumin (34,000), does not appear until after twenty-four hours. Similar tests made in the refrigerator showed globulin present in the dialysate in traces after forty-eight hours, and in large amounts after seventy-two hours. This indicates that even at this temperature by forty-eight hours the integrity of the capsule has been damaged.

D. Quantitative tests of the total nitrogen in the dialysate after various intervals were made by the micro-Kjeldahl method of Koch and

McMeekin.[36] In one series of these tests the same lens was transferred to successive test tubes after two hour periods. When this was done the rate of dialysis was found to be fairly regular, at least in the first twelve hours, being approximately 0.140 mg. per two hour period. When the lens was left in one tube for longer periods, the accumulation of albumin in the dialysate retarded further dialysis, so that the rate became slower. Similar results were obtained when the total organic matter in the dialysate was estimated by titration with potassium permanganate.

E. When the same tests were made with decapsulated lenses, positive reactions for albumin, globulin and glutathione were obtained in

TABLE 4.—*Total Nitrogen in Dialysate of Intact and Decapsulated Lenses*

Lens	Dog	Rabbit	Sheep
Encapsulated	0.102 mg. N	0.207 mg. N	0.254 mg. N
Decapsulated	0.510 mg. N	0.918 mg. N	1.089 mg. N

the surrounding fluid after fifteen minutes. These greatly increased amounts of nitrogenous organic matter at this period, as compared with that in the dialysate of lenses in the capsule, give further evidence of a definite protective action of the capsule against loss of lens proteins.

F. Quantitative estimations of total nitrogen in the surrounding fluid of intact and decapsulated lenses gave the results shown in table 4.

From four to five times as much nitrogenous organic matter leaves the decapsulated lens as leaves the intact lens, thus affording further evidence of the protective action of the capsule of the lens for these substances. The factor of autolysis would be the same with and without the capsule.

36. Koch and McMeekin: Total Nitrogen by Direct Nesslerization After Micro-Kjeldahl, J. Am. Chem. Soc. **46**:2066, 1924.

G. Dialysis of glutathione through the capsule of the lens showed the following:

Conditions.—Four beef lenses were dialyzed at icebox temperature in tubes containing 15 cc. of physiologic solution of sodium chloride. The lenses were removed at the end of twenty-four hours and changed to another set of similarly prepared tubes. This was repeated after forty-eight, seventy-two, ninety-six and one hundred and twenty hours. The dialysate (after removal of the lens) was used for determinations of glutathione. Chart 1 represents the quantity of glutathione found in the dialyzing medium at the end of each dialyzing period.

Interpretation.—The rate of dialysis in the four lenses is fairly constant. The rise in the graphs during forty-eight hours probably represents the combined effects of degenerative changes in the capsule

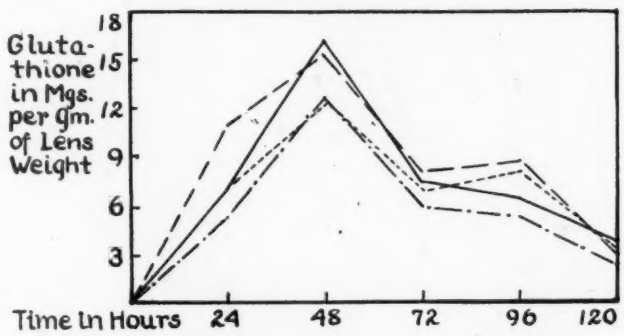


Chart 1.—The quantity of glutathione that dialized out through the capsule of the lens during the different periods. The dash line indicates lens no. 4; the continuous line, lens no. 1; the dotted line, lens no. 3, and the dash-dot line, lens no. 2.

and freeing of glutathione from a combination with the lens proteins as these are broken down. The fall after this time seems to show that most of the substance had escaped from the lens.

IV. FACTORS INFLUENCING PERMEABILITY

A. Modifying Effect of Various Substances on Permeability.—Conditions: Paired sheep lenses from the same animal were placed, one in pure Ringer's solution as a control, and the other in Ringer's solution with the test substance added. After five hours, the dialysates were analyzed for their nitrogen content (table 5).

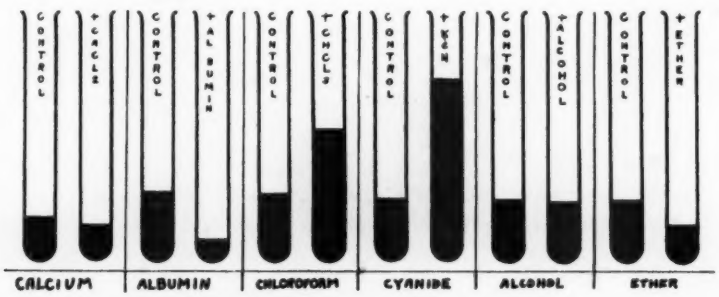
Interpretation: Permeability is decreased by calcium, albumin and ether; increased by chloroform and potassium cyanide, and unchanged by alcohol.

B. Permeability in Relation to p_H.—Sheep lenses of approximately the same weight were placed in McIlvaine's [37] buffer solution (composed, according to the p_H desired, of varying proportions of 0.2 molar of disodium acid phosphate and 0.1 molar of citric acid). The solutions in the test tubes were buffered at 0.2 intervals from p_H 6 to p_H 8. There was a definite increase of permeability toward the acid side. The average nitrogen content in dialysates below p_H 7.2 was 0.437 mg. and above p_H 7.2, 0.301 mg. No opacities developed in these lenses during fifteen days of observation.

C. Permeability in Relation to Osmotic Pressure.—Sheep lenses of approximately the same weight were placed in solutions of sodium

TABLE 5.—*Effect of Various Substances on Permeability*

Total Nitrogen in Dialysate of Control Lens, Mg.	Substance Added	Total Nitrogen in Dialysate of Treated Lens, Mg.
0.214	Calcium chloride (to 0.3%)	0.182
0.353	Albumin (0.343 mg. N content)	0.101
0.343	Chloroform (5 drops to 15 cc.)	0.686
0.316	Potassium cyanide (to 0.25%)	0.948
0.316	Alcohol (15 drops to 15 cc.)	0.308
0.343	Ether (15 drops to 15 cc.)	0.192



chloride, varying by 0.2 per cent, from 0.8 to 3 per cent. Approximately the same amount of nitrogen was recovered from each dialysate. The osmotic pressure of electrolytes hence does not affect the permeability of the capsule to nitrogenous organic matter.

D. Permeability in Relation to the Size of the Lens.—The smaller the lens, the greater is the permeability of its capsule to nitrogenous organic matter (table 6).

E. Permeability in Relation to Age.—Conditions of Experiment: Unborn calf lenses and adult sheep lenses that were approximately in

37. McIlvaine, T. C.: A Buffer Solution for Colorimetric Comparison, J. Biol. Chem. **49**:183, 1921.

the same weight range were dialyzed for five hours in Ringer's solution under identical conditions. The nitrogen content of the dialysate was then determined.

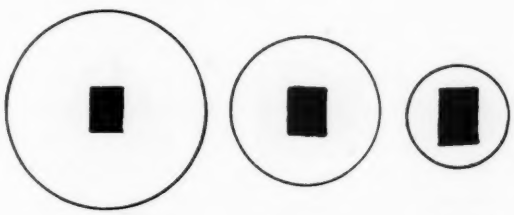
The permeability of the capsule to the nitrogenous organic matter contained in the lens is apparently slightly decreased with age.

V. THE PERMEABILITY OF CALF AND BEEF LENSES TO SUBSTANCES OF VARYING MOLECULAR SIZE

Conditions.—Lenses of approximately full term unborn calves (average weight, 0.7364 Gm.) were compared to beef lenses under the conditions of experiment II, except that all the determinations were made

TABLE 6.—*Permeability of Lenses of Varying Size*

Species	Lens (Average Weight, Gm.)	Area (Calculated, Sq. Cm.)	Nitrogen Content of Dialysate, Mg.	Ratio of Dialyzed N to Area
Ox	2.2485	7.6913	0.4300	0.056
Sheep	0.8744	4.0978	0.3065	0.075
Rabbit	0.3728	2.3213	0.2128	0.095



within a five hour period, when the capsules had presumably undergone practically no change (tables 8 and 9 and charts 2 and 3). It was impossible to obtain a series of lenses from animals of varying known age, so these two types were chosen as representing a fairly constant difference of age.

Interpretation.—While the beef lens absorbed absolutely a slightly greater amount of each reagent, the ratio of permeability was definitely greater for the calf lens in every determination for both reagents. For sodium salicylate it was usually twice as great, while for fluorescein it was from three to five times as great.

VI. PERMEABILITY OF CATARACTOUS LENSES

A. Permeability for Substances Contained in the Lens.—Conditions: The lenses mentioned in table 10 were dialyzed for five hour periods, and the total nitrogen in the dialysate was determined.

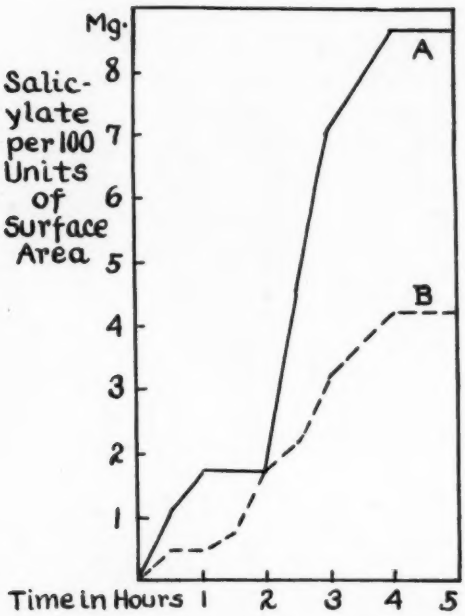


Chart 2.—The amount of sodium salicylate that dialyzed into the lens through the capsule. Calf (*A*) and beef (*B*) lenses are compared, and the salicylate is stated in terms of milligrams per hundred units of surface area. Sodium salicylate in a dilution of 1 : 1,000 was used for dialysis.

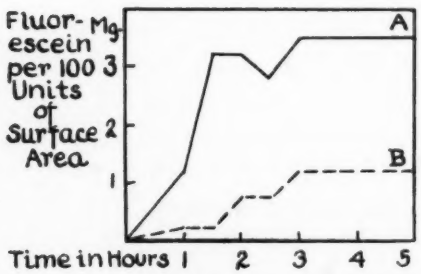


Chart 3.—The amount of fluorescein that dialyzed into the lens through the capsule. Calf (*A*) and beef (*B*) lenses are compared, and the fluorescein is stated in terms of milligrams per hundred units of surface area. Fluorescein in a dilution of 1 : 1,000 was used for dialysis.

In rabbits, the dialysate of the normal lens contains less nitrogen than the dialysate from incipient naphthalene cataract, but more nitrogen than the dialysate from mature naphthalene cataract.

Mature cataracts in human beings show about the same permeability as the normal rabbit's lens.

TABLE 7.—*Permeability in Relation to Age*

Lens	Average Weight, Gm.	Calculated Area, Sq. Cm.	Nitrogen Content of Dialysate, Mg.	Ratio of Dialyzed Nitrogen to Area
Adult sheep	0.9146	4.2224	0.2536	0.060
Unborn calves	0.7230	3.6100	0.2389	0.066

At 20 C. TABLE 8.—*Permeability of Calf and Beef Lenses for Sodium Salicylate*

Time in Hours	Average Weight in Gm.		Average Surface Area in Sq. Cm.		Mg. of Salicylate in the Lens		Ratio of Permeability (P/A)	
	Calf	Beef	Calf	Beef	Calf	Beef	Calf	Beef
½	0.7364	2.2485	3.7462	7.6913	0.04	0.04	0.0107	0.0052
1	0.7364	2.2485	3.7462	7.6913	0.063	0.04	0.0167	0.0052
1½	0.7364	2.2485	3.7462	7.6913	0.05	0.05	0.0163	0.0065
2	0.7364	2.2485	3.7462	7.6913	0.06	0.125	0.0160	0.0162
2½	0.7364	2.2485	3.7462	7.6913	0.08	0.166	0.0443	0.0216
3	0.7364	2.2485	3.7462	7.6913	0.08	0.25	0.0695	0.0324
4	0.7364	2.2485	3.7462	7.6913	0.125	0.33	0.0882	0.0429
5	0.7364	2.2485	3.7462	7.6913	0.125	0.33	0.0882	0.0429

At 20 C. TABLE 9.—*Permeability of Calf and Beef Lenses for Fluorescein*

Time in Hours	Average Weight in Gm.		Average Surface Area in Sq. Cm.		Mg. of Fluorescein in the Lens		Ratio of Permeability (P/A)	
	Calf	Beef	Calf	Beef	Calf	Beef	Calf	Beef
½	0.7364	2.2485	3.7462	7.6913	0.025	0.0062	0.0067	0.0008
1	0.7364	2.2485	3.7462	7.6913	0.05	0.025	0.0134	0.0032
1½	0.7364	2.2485	3.7462	7.6913	0.12	0.03	0.0320	0.0039
2	0.7364	2.2485	3.7462	7.6913	0.12	0.05	0.0320	0.0065
2½	0.7364	2.2485	3.7462	7.6913	0.10	0.05	0.0268	0.0065
3	0.7364	2.2485	3.7462	7.6913	0.13	0.10	0.0347	0.0130
4	0.7364	2.2485	3.7462	7.6913	0.13	0.10	0.0347	0.0130
5	0.7364	2.2485	3.7462	7.6913	0.13	0.10	0.0347	0.0130

None of the dialysates for the five hour period gave a positive reaction for globulin.

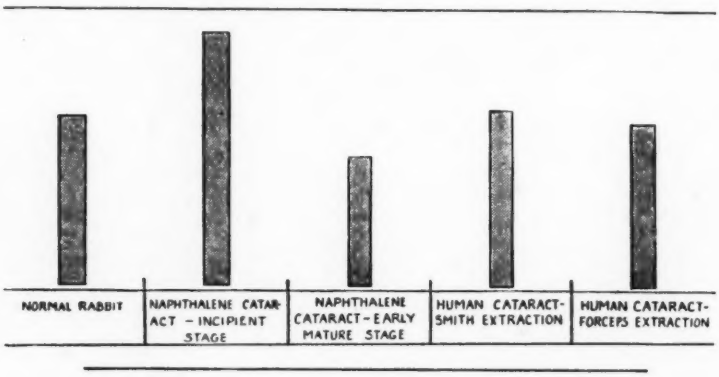
B. Permeability of Cataractous Lenses for Substances Absorbed from Without.—Conditions: Senile cataractous lenses from human beings were placed in 5 per cent sodium salicylate immediately after intracapsular extraction and kept at room temperature.

Cataractous lens substance absorbs about as much salicylate as would be calculated for beef lenses of similar size.

C. Permeability During Life of the Normal Lens and the Lens with Naphthalene Cataract.—As substances for experiments in vivo, sodium salicylate and fluorescein sodium were chosen because both could be determined quantitatively in minute amounts and both pass freely into the aqueous from the blood stream. A few other substances, chiefly dyes, were also employed.

TABLE 10.—*Permeability of Cataractous Lenses for Nitrogenous Matter*

Character of Lens	Average Weight, Gm.	Area Calculated, Sq. Cm.	Nitrogen Content of Dialysate, Mg.	Ratio of Dialyzed Nitrogen to Area
Normal rabbit (average of 8 lenses)	0.3728	2.3213	0.2128	0.091
Naphthalene cataract, incipient stage (8 lenses)	0.49551	2.8063	0.3845	0.137
Naphthalene cataract, early mature stage (4 lenses)	0.7220	3.6066	0.2527	0.070
Human cataract (1), Smith extraction	0.2915	1.9701	0.1880	0.095
Human cataract (1), forceps extraction	0.2670	1.8581	0.1650	0.089



Eleven rabbits were given from 10 to 15 cc. of 5 per cent sodium salicylate by stomach tube daily for from one to five days. Seven of these were normal animals, and three showed complete or almost complete opacity of the lenses as a result of naphthalene feeding. The amount of salicyl in the aqueous of both eyes was estimated directly with ammonio-ferric alum by comparison with a color scale. That in the lenses was estimated in the same way after extraction with anhydrous ether.

In normal animals the variations in relation between concentration of the drug in aqueous and lenses are accounted for by the time after feeding at which the examination was made. The aqueous showed its highest concentration after from one to two hours, the amount being markedly reduced or altogether absent after twenty-four hours. None was found in the lens after one day's feeding and a trace after two days, while after three days the amount was more constant, whether the examination was made one or twenty-four hours after the last

feeding, being usually from 1:30,000 to 1:64,000. No reason for the negative findings in the rabbit after five days' feeding can be given. No increase in the amount of salicyl in lenses with naphthalene cataract was found. In one animal the amount was about the same as in normal animals, while in two others none was present in the lenses after four days' feeding. This suggests either a slight decrease in permeability of the capsule of the lens or a decreased ability of the lens substance to absorb the drug.

TABLE 11.—*Permeability of Cataractous Lenses for Sodium Salicylate*

Time	Weight (After Dialysis)	Method of Extraction	Salicylate Absorbed, Mg.	Estimated Maximum Absorption Similar Weight Beef Lens
48 hours	0.298	Erisphake	0.95	0.9277
	0.320	Capsule forceps	1.10	0.9962

TABLE 12.—*Permeability During Life of Normal Cataractous Lenses for Salicylate*

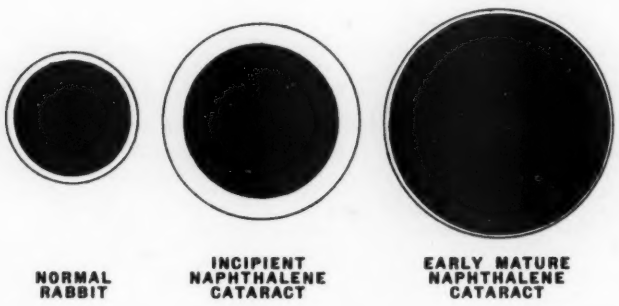
No.	Data of Dosage and Precedure	Amount in Aqueous	Amount in Lenses
	Normal Rabbits		
1	Fed twice daily for 2 days; died; examined 8 hours post mortem	1:16,000	1:30,000
2	Fed for 4 days; examined 1 hour after last feeding	1:20,000	1:40,000
3	Fed for 4 days; examined 1 hour after last feeding	1:8,000	1:30,000
4	Fed twice daily for 3 days; died; examined 12 hours post mortem	1:64,000	1:5,000
5	Fed for 5 days; examined 24 hours after last feeding	Negative	Negative
6	Fed twice daily for 3 days; aqueous examination 1½ hours after last feeding; lens 3 days later	1:2,400	1:64,000
7	Fed twice; examined 16 hours after last feeding	1:64,000	Negative
8	Fed 3 doses in 2 days; examined 12 hours post mortem	1:20,000	Trace
	Rabbits with Naphthalene Cataract		
9	Fed for 4 days; examined 16 hours after last feeding	1:50,000	Negative
10	Fed for 4 days; examined 1½ hours after last feeding	1:25,000	Negative
11	Fed for 5 days; examined 24 hours after last feeding	1:100,000	1:25,000

Eight rabbits were given subcutaneous injections of from 3 to 4 cc. of 3 per cent fluorescein sodium for from three to six days. Four animals were normal, and four showed naphthalene cataract. The fluorescein in the aqueous was estimated directly by comparison with a color scale in the beam of an arc light with a corning filter no. G.986, which permits the detection of fluorescein in dilutions of 1:36,000,000. That in the lenses was estimated by the same method after extraction for one hour in 8 cc. of water, the solid particles then being removed by vigorous centrifugation. The amount present in the aqueous of normal animals varied between 1:1,200,000 and 1:7,000,000, while none was detected in the lenses. In one animal given only one injection that in the lenses was from 1:350,000 to 1:1,500,000. In one animal

by vein, a trace of fluorescein was found in the lens after two hours. Of the three animals with naphthalene cataract, two showed no fluorescein in the lens, one a trace (less than 1:3,600,000) and one 1:350,000. This animal showed an unusually high concentration of fluorescein in the aqueous, 1:200,000, which was examined an hour after the sixth injection. The findings, though dealing with amounts too small to be compared with great accuracy, certainly indicate no greater absorption of fluorescein by the lenses with naphthalene cataract, such evidence as is given pointing, in fact, to a lessened absorption by such lenses.

TABLE 13.—*Absorption of Water by Lenses with Naphthalene Cataract*

Lens	Normal Rabbit	Normal Rabbit (Decapsulated)	Incipient Naphthalene Cataract	Early Mature Naphthalene Cataract
Original weight	0.3788 Gm.	0.3335 Gm.	0.4956 Gm.	0.7220 Gm.
Change in weight after 10 hours..	+0.0415 Gm.	—0.0504 Gm.	+0.1361 Gm.	+0.0256 Gm.



VII. WATER-ABSORPTION BY THE NORMAL LENS AND LENSES WITH EXPERIMENTAL CATARACT

A. Fresh sheep lenses show no change of weight in 1.4 per cent saline. Duke-Elder estimated the osmotic pressure of the lens as equivalent to 1.2 per cent saline, which is in practical accord with this finding.

B. Toxic substances can cause the lens to swell. Whereas the normal rabbit lens weighs from 0.3174 to 0.4680 Gm., the clear lenses of a rabbit dying of prolonged menthol poisoning averaged 0.5135 Gm. in weight.

C. Normal and cataractous lenses were placed in Ringer's solution, and the change in weight after ten hours was noted.

It will be seen from table 13 that the immature naphthalene cataract shows an increase in weight as compared with the normal lens, but that it is capable of a further increase in weight while in Ringer's

solution. These changes are probably based on an increase in osmotic pressure due to breaking down of the lens proteins. The mature naphthalene cataract, which is much more swollen to begin with, shows little further increase in weight during the experiment, having apparently already reached its maximum osmotic pressure as a result of more complete break-down.

D. Of ten ox lenses placed in Ringer's solution for six days, all but the smallest developed water fissures. The total nitrogen in the dialysate for this period for a lens weighing 2.045 Gm. was 5.805 mg., and for a lens without water fissures, weighing 1.7705 Gm., it was only 3.913 mg. This may mean that the smaller and hence younger lens is less susceptible to the breaking down of its proteins.

Lenses of unborn calves that were placed in Ringer's solution for ten days did not develop water fissures. Their absorbing power for water, however, seems to be equal, if not slightly more than, that of adult lenses. In five hours, the lenses of unborn calves gained an average of 0.1469 Gm., while the lenses of adult sheep gained 0.1281 Gm. This difference may be interpreted as due to a uniform absorption of water throughout the lens in younger animals, while in older animals a lessened ability to absorb water by the lens fibers allows the collection of water in the interfibrillar spaces.

E. In adult lenses, the entrance of water promotes disintegration. When placed in Ringer's solution, which is hypotonic to the lens, the majority of adult lenses develop water fissures in three days, more markedly in the anterior portion of the lens. However, lenses placed in buffer solutions in a range of from p_H 6 to p_H 8 with an osmotic pressure approximately equivalent to 1.5 per cent saline remained clear and without water fissures for over two weeks. Lenses on the acid side tend to develop a slight subcapsular opacity on the first day, which later clears.

F. Opacities of the lens that may be preserved indefinitely may be produced by adding a few drops of chloroform to the solution containing the lens. These lenses do not show water fissures until after about three weeks, since the rapid diffusion of albumin from the lens maintains a high osmotic pressure in the surrounding solution. After a month in the solution, these artificial cataracts still contain some glutathione, indicating that the loss of glutathione follows rather than initiates the process of opacification.

CONCLUSIONS

1. The normal capsule is freely permeable to water, electrolytes and substances of higher molecular weight, such as sodium salicylate and fluorescein.

2. In experiments with sodium salicylate diffusion into the lens was the same with and without the capsule.

3. With substances of larger molecular weight, albumin, glutathione and globulin, a certain barrier to dialysis is exerted by the capsule of the lens. Since albumin may be detected after dialysis for two hours, it is probable that some albumin passes through the normal capsule, but in such minute amounts that an equilibrium is maintained between the aqueous and the lens substance. Apparently no globulin passes through the capsule until postmortem changes have occurred.

4. The fact that postmortem changes were not responsible for the absorption of sodium salicylate and fluorescein is proved by the experiments in which these were given during life.

5. Young lenses were shown to be definitely more permeable to the substances tested than normal lenses of older animals. The difference was slight in substances dialyzing from within the lens out, but marked for sodium salicylate and fluorescein.

6. In five cataractous lenses from human beings extracted within the capsule, permeability of the capsule for various substances was approximately the same as that of the normal rabbit lens.

7. No evidence of "selective permeability" was found, the only factor influencing permeability being the molecular size of the substances tested.

8. Within a range much greater than that possible during life, variations of neither osmotic pressure nor hydrogen ion concentration were effective in producing cataract in vitro. This seems to invalidate the assumption of Duke-Elder that these factors are of importance in the genesis of cataract. The other factor which he considered of importance, ultraviolet rays, need not be considered in view of the work of Vogt and others previously quoted.

9. The fact that sodium salicylate did not penetrate the nucleus of normal beef lenses till after twenty-four hours in the incubator indicates the sluggish metabolism of this portion of the lens, which may be considered a factor in the genesis of nuclear sclerosis.

10. In mature naphthalene cataract no increase in permeability of the capsule was found. The swelling of the lens in this condition can be due only to the absorption of water induced by an increased osmotic pressure of the lens substance. This is apparently the result of breaking down of the lens proteins into substances of smaller and more numerous molecules. This seems to offer a satisfactory explanation of the findings of Schmerl and Thiel, as such a break-down would involve more active oxidative processes. The finding of a positive reaction to sodium nitroprusside in the aqueous of such lenses and of an increase

in organic matter escaping through the capsule during the incipient stage of naphthalene cataract may be explained by the freeing of glutathione and other substances in the processes of decomposition. This is in line with the swelling observed in the intumescent stage of senile cataract and the loss of solids in this and later stages.

11. The degenerative changes shown by histologic methods in the capsule of naphthalene cataract do not indicate an increased permeability in view of our findings.

12. In view of the foregoing findings with respect to permeability of young and old lenses and lenses with experimental cataract, any theory of the genesis of cataract based on increased permeability of the capsule would seem to be without foundation. Traumatic cataract, which is used as an example in favor of this theory, may be considered as a swelling and separation of the lens fibers deprived of the covering that normally holds them in close apposition, allowing them to absorb more water and permitting the loss of their globulin content. In this condition there is no question of increased permeability of the capsule, but an actual loss of part of the capsule itself.

ABSTRACT OF DISCUSSION

DR. DERRICK T. VAIL, Cincinnati: I regret that my chemical training is such that I am unable to discuss intelligently the more complex nature of this admirable review of biochemistry of the lens, and particularly the convincing experimental work on the permeability of the capsule of the lens. I sincerely hope that wiser heads here will discuss this phase and relieve me of the embarrassment of revealing my ignorance.

The *ultima Thule* of this work and similar studies, as indicated by the essayists, is the pathogenesis of cataract. Interesting as these preliminary studies may be to the ophthalmophysiologist, the clinical ophthalmologist will be inclined to ignore them until the goal is reached. And yet, as I hope to show later, the studies so far undertaken have already partially settled, at least, a certain clinical controversy regarding hypermature cataract with which the father of one of the essayists, Dr. Harold Gifford, was engaged.

The approach to the solution of the cause of cataract has been, until fairly recent times, strictly anatomic and clinical. Histopathology of the lens has proved to be most unsatisfactory, and clinical observation previous to biomicroscopy was restricted to a study of the types of lens opacities and their progression. Extracapsular operations were the rule, and thus lens material removed for study was either macerated or limited to the nucleus. It is only since the advent of the slit-lamp and microscope, and especially since the great increase in microchemical methods of analysis, that we have started on the path of that which will eventually prove to be, I am certain, the cause of cataract and its logical medical cure.

We shall expect, therefore, from now on, an ever increasing number of chemical investigations on the lens and its capsule, and it behooves those of us who are clinicians only, and not laboratory men, to seize the opportunity given us by this essay to learn at least the fundamental chemistry of the lens.

The theory held by many workers on this perplexing question, namely, that cataract is caused by an increased permeability of the capsule of the lens, seems to

have suffered a severe setback by Drs. Gifford and Lebensohn. However, what theory they propose in its place is not quite clear.

As I understand it, the metabolism of the normal lens is an internal one due to its avascular structure, thus accounting for the importance of glutathione and beta crystallin. The combination of the reaction between glutathione and beta crystallin, and vice versa, results in a balanced autoxidation mechanism which, unless something intervened, might be considered as a form of perpetual chemical motion.

The authors support by their experiments the premise that there is a decrease in the permeability of the capsule of the lens with age. I am sure that all of us who have operated on a hypermature tumescence of morgagnian cataract will agree with this finding, for not only is such a cataract swollen and globular, but its contents seem to be under a high pressure, so that stripping of the capsule results in the extrusion of milky contents and shriveled nucleus like a miniature explosion. The increase in fluid content might be explained by an increase in the osmotic pressure within the lens due to an increase of calcium salts and a decreasing amount of glutathione. As the permeability of the capsule of the lens decreases there should be an increase in the products of disintegration within the lens, leading to the formation of cholesterol, tyrosine and leucine. Rötth [38] has recently shown that tyrosine and insoluble cystine injected into the anterior chambers of rabbits produce a violent iritis. If there were an increased permeability of the capsule of the lens with age, one would naturally expect a release of the toxic products of disintegration into the aqueous, resulting in iritis and secondary glaucoma.

Verhoeff, in discussing Dr. Arnold Knapp's [39] paper on this subject, said that he was sure that the fluid of morgagnian cataract was toxic, for when there is a spontaneous rupture of the capsule, as sometimes happens in these cases, the fluid produces a characteristic reaction in the eye which is slowly progressive and will ruin the eye. He also said that it is not justifiable to conclude that the fluid of a morgagnian cataract is not toxic because it causes no serious reaction after extraction of the cataract, for when the cataract is removed the anterior chamber becomes obliterated and practically none of the morgagnian fluid is left in the eye.

A case that I reported [40] is an excellent example of the toxic effect of degeneration of the lens protein, which is active only when the capsule is ruptured.

It is interesting to note that Dr. Harold Gifford and Dr. Herman Knapp supported the theory of absorption of toxic lens products through the intact capsule as a cause of glaucoma in these cases. Dr. Arnold Knapp took the opposite stand. Dr. Sanford Gifford will probably find himself allied with the latter, and thus we see the unusual spectacle of two famous sons pitted against two famous fathers.

In the cases of four young adults, I have seen a perforating wound of the lens lead to a diffuse opacification in twenty-four hours. From three to four days later, the opacity began to clear, and in all four the vision eventually became normal. Only the track of the foreign body remained opaque, and in one case a small area of the lens immediately surrounding the end of the path just anterior to the capsule was also opaque, and has remained in *status quo ante* for three years. These cases prove that even if the capsule of the lens is artificially rendered more permeable

38. Rötth, A.: Arch. f. Ophth. **122**:34, 1929.

39. Knapp, Arnold: Observations on Glaucoma in Morgagnian Cataract, Tr. Am. Ophth. Soc. **24**:87, 1926.

40. Vail, D. T.: Endophthalmitis from Retained Foreign-Body Phacocyst, Arch. Ophth. **56**:5 (Jan.) 1927.

to the aqueous, chemical reactions within the lens in healthy youthful subjects are sufficiently powerful in certain unexplained cases to regenerate transparency.

Apparently, this paper is but a forerunner of future studies. It is hoped that the investigators will have access to plenty of entire human lenses, which, in these days of intracapsular operations, should not be difficult, so that the study of permeability of the capsule of the lens can be carried out through all the stages of cataract maturity.

DR. JONAS FRIEDENWALD, Baltimore: I think that the Section is to be congratulated on having presented before it this most important paper, one that seems to tend toward the solution of some of our most difficult problems. I am gratified to hear that Dr. Gifford and Dr. Lebensohn have confirmed, by a totally different technic, my own findings of three years ago in relation to the permeability of the capsule of the lens.

There is, however, one point I wish to raise in the interpretation of these findings. The experiments of Dr. Gifford and Dr. Lebensohn consisted in placing an intact lens in a solution, and then testing how much of the solute penetrated into the lens after various intervals. In order that the solute should be taken up by the lens in any quantity, it must (1) diffuse across the capsule, (2) diffuse across the cell boundary of the lens fibers, and (3) be absorbed by the protoplasm of the fibers. There is no reason to believe that the rates of these three processes taken separately should be equal. In such a three-stage process taken all together, the slowest element is the one that controls the total rate. In one of the experiments reported, the authors found that the rate of absorption of salicylate by the decapsulated lens was the same as that by the lens in the capsule It is to be inferred that what the authors were measuring in their experiments on the intact lens was not the permeability of the capsule, but the rate of absorption by the lens fibers. It is clear, however, that the permeability of the capsule must be at least as great as the values which they found, though possibly much greater.

These experiments are, therefore, adequate to lay at rest the theory that increased permeability of the capsule is the cause of cataract. The experiments demonstrate that the capsule is freely permeable to water, electrolytes and other crystalloids, and that no increase in permeability of the capsule can enhance the advent of these substances into the interior of the lens.

DR. SANFORD R. GIFFORD: The gist of our experimental results is that the normal capsule of the lens is fully permeable to substances of quite high molecular weight and, of course, to water and electrolytes. This makes necessary the assumption of a free interchange of the substances necessary for nutrition and oxygen consumption by the lens fibers during their life and the elimination of their waste products through the normal capsule of the lens. This was shown by Friedenwald, and our work agrees with his in all essentials. The method of studying permeability in the intact lens instead of in the isolated capsule was chosen as more nearly approaching normal conditions and being less open to the objection of possible artificial damage to the capsule, although Friedenwald's careful work seems to have eliminated this factor. It is recognized, as Friedenwald has pointed out, that what we are measuring is the absorption of the lens fibers through the capsule, except in the case of substances already present in the lens.

It was found that this permeability does not increase with age or the onset of cataract, but, on the contrary, seems to decrease definitely. Whether this decrease is enough to prevent proper nutrition from reaching the lens and hence to hasten the death of the lens fibers, with resulting cataract formation, cannot now be stated, but such an effect, as Friedenwald has suggested, is easily conceivable. It was thought important to determine this, because many facts concerning cataract have

been interpreted on the theory that increased permeability of the capsule of the lens causes cataract. This theory evidently arose from the clinical observation of cataract after damage to the capsule of the lens and has caused many ophthalmologists to interpret glass-blowers' cataract as due to increased permeability of the capsule, the detachment of the zonular lamellæ as seen in such cases being considered evidence in this direction. The increased consumption of oxygen of the cataractous lens shown by Schmerl and Thiel was explained on this theory, as was the occurrence of naphthalene cataract, in which changes in the capsule may be demonstrated histologically. However, when it is known that such increased permeability does not occur, it seems possible to explain all these phenomena in other ways. In glass-blowers' and roentgen cataract, damage has evidently been done both to the capsular epithelium and to the growing lens fibers, especially the nuclei in the equatorial zone. Such damage causes their premature death, with a resulting breaking down of the lens proteins, swelling of the lens fibers by increased osmotic pressure and opacity. The same may be said of naphthalene cataract, the reason for this increased consumption of oxygen by such lenses being the broken down lens substance, and not an increased permeability of the capsule. The same may be true of senile cataract, in which the living lens fibers at the periphery die or cease to be formed. The decreased permeability of the capsule may hinder, but cannot prevent, the escape of broken down lens proteins, which accounts for the loss of weight in such lenses. What occurs in traumatic cataract is quite different. In this condition the mechanical pressure of the capsule, which holds the lens fibers together and limits their swelling, is removed over a greater or a lesser area. The fibers spring apart, their delicate sheaths are broken, and they swell freely according to the amount of fluid absorbed. This is what happened in our experiments with decapsulated lens, in which large amounts of nitrogenous matter passed freely into the surrounding fluid.

An important distinction must be made between changes in the clear lens with age and changes in the cataractous lens. While the clear lens increases in weight and solid constituents, when opacities of the lens occur, the opposite process takes place, and the lens loses in solid constituents. Something has happened, presumably the death of the peripheral living lens fibers, which sets off this process from the normal events of the clear senile lens. The exception to this is in pure nuclear sclerosis with its various stages of yellow to brown cataract, and probably also black cataract. Here the normal increase in weight and solid constituents goes on, so that this may be considered a true form of senile lens damage. The fact that cortical or subcortical cataract is at least as common, or more common, than advanced nuclear sclerosis in old age apparently means that the process of breaking down of the lens proteins and opacification of the cortex, which must be considered pathologic, does occur commonly in old age, as do such other pathologic processes as arteriosclerosis.

Clinical Notes

SUBSEQUENT HISTORY OF RETAINED NUCLEUS AFTER CATARACT EXTRACTION

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The subsequent history of retained nucleus after attempted cataract extraction is a subject about which little is stated in the textbooks. The report of the two following cases may therefore be justified.

REPORT OF CASES

CASE 1.—W. E. G., aged 31, was seen on July 31, 1923, stating that the vision in the right eye had been failing for two years, and in the left eye for six months. There was a soft cataract in the right eye, and vision was reduced to perception of hand movements. The left eye presented a posterior cortical cataract, and vision was only 10/200.

At operation on August 8, on making the section, fluid vitreous immediately escaped and the scleral envelop collapsed. No opening could be made in the capsule with either the toothed forceps or the cystotome. The Reisinger hook and loop were then introduced, but only some of the cortex could be removed. The collapsed eyeball was filled with physiologic solution of sodium chloride. The operation was followed by a moderate reaction, and the patient was treated with injections of milk. After the incision had healed, the cataract could be seen displaced backward, floating freely in the vitreous on moving the eye, but still attached below. With a correcting glass vision was 20/70; there was moderate ciliary congestion, and the iris was fair. The cortical masses then partly absorbed, but the vitreous opacities remained.

On September 21 the eye became more red, with a dilated pupil and a cloudy cornea. Vision was reduced to 5/200. Deposits were present on the posterior surface of the cornea. Tension was 41 (Schiötz). On September 26, the nucleus appeared in the anterior chamber. A keratome incision was made at the limbus down and out, the wound was enlarged with curved scissors and the nucleus was extracted without any loss of vitreous. Recovery was rapid. On December 4, the eye was white, and vision was 20/20.

The patient was then not seen again until Jan. 4, 1932, when the eye was found to have remained healthy, and vision with a correcting glass was 20/20. Within the pupil there was a thickened capsular margin, but the vitreous was perfectly clear.

CASE 2.—R. L. H., aged 56, was seen on Oct. 16, 1924. Two days previously, a foreign body had passed through the iris and the lens of the left eye and lodged in the vitreous body; it was extracted with the giant magnet, by the anterior route around the lens, without any mishap. On November 3, the eye had become painful and hard; vision was reduced to perception of hand movements; the cornea was dull; there were posterior corneal deposits; the iris was tremulous, and there was some cortex in the pupil. A coherent cataractous mass protruded through the wound in

the posterior capsule of the lens into the vitreous where it moved with the eye. Sudden swelling of the lens undoubtedly had caused a stretching of the old wound in the posterior capsule and a displacement of some of the lens matter into the vitreous, which then caused secondary glaucoma. As the eye did not respond to medical treatment, an incision was made at the limbus on November 4; fluid vitreous immediately escaped, and the depth of the anterior chamber did not change. The cornea became clear, and as the pupil was dilated, an examination of the interior of the eye could be made. The nucleus was found lying at the bottom of the vitreous chamber. The patient was placed on his face for two hours every day, in the hope that the nucleus would be brought forward into the anterior chamber. While it presented in the pupillary area, the nucleus would then fall back again in its old place. On December 19, it was still visible at the bottom of the vitreous, but it seemed to be splitting up and absorbing in its periphery. Tension was normal. With a correcting glass vision was 10/200. At the end of two months the nucleus could no longer be seen, there was no other change in the eye and the vitreous opacities were still present. With glasses the sight improved gradually to 20/30. The patient was not seen again until June 15, 1931, when vision in the left eye was 20/30. The eye seemed perfectly sound. The vitreous was clear and there were some capsular remnants in the pupillary area below; on careful search with a maximally dilated pupil, no trace of the nucleus could be discovered.

COMMENT

The value of salt solution in a collapsed eyeball (case 1), as pointed out by H. Knapp many years ago, cannot be overstated. It permits proper union of the incision to take place, and protects the eye from infection until the vitreous is replaced by whatever substitute forms. This case also shows that if the nucleus can travel, it will sooner or later come into the anterior chamber where its elimination is easy.

In case 2 the wound of the anterior lens capsule must have closed, or for some other reason the swelling lens escaped posteriorly into the vitreous. That the combination of lens tissue and vitreous is prone to set up disturbance, and especially glaucoma, is well known. The absorption of the nucleus in the vitreous chamber without causing any damage to the eye, even if slow, was fortunate.

It is generally accepted that in the cataract operation in adults the nucleus must be extracted; the retained cortex will take care of itself or, if troublesome, can be treated by further operation. That there may be recovery from a retained nucleus with good resulting vision, as in the two cases reported, is, I hope, of interest.

Ophthalmologic Review

EDITED BY DR. FRANCIS HEED ADLER

CELLULAR PERMEABILITY IN RELATION TO OPHTHALMOLOGY

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Studies of cellular permeability in both animal and plant tissues have been carried on by a number of workers for the past fifty years. Most of these investigations have been undertaken in relation to specific problems in animal or plant physiology. It is only recently that the subject of cell permeability has become recognized as an independent and fairly well limited field in the general domain of physiology. The general literature on cellular permeability has recently been subjected to a thorough review by Gellhorn.[1] The object of the present review is to sketch the main outlines of the results of these investigations in general, and to enumerate the applications that have been made of this field of study in relation to the physiology of the eye.

METHOD

A variety of technics have been elaborated to test the permeability of cells and tissues. The first and most direct method consists in placing the cells or tissues to be tested in an environment containing the test substance, with subsequent examination, either visual or chemical, to discover whether the foreign substance has, or has not, entered the cells. Several difficulties exist in relation to this technic. The cell boundary may be freely permeable to some substance which is, nevertheless, negatively adsorbed by the cell protoplasm, so as to be present within the cell in only an immeasurably small quantity. On the other hand, the test substance may be positively adsorbed by the cell boundary, and be present in large amounts on chemical analysis of the cell without ever having penetrated into its interior. Finally, it is a general rule that injured or dying cells are more freely permeable than are normal cells, and under experimental conditions substances may be found to enter the interior of cells from which, under physiologic conditions, they would be excluded. A refinement of this direct method consists in the use of structures or pigment normally occurring within

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1. Gellhorn, E.: Das Permeabilitätsproblem, Monographien aus dem Gesamtgebiet der Physiologie der Pflanzen und der Tiere, Berlin, Julius Springer, 1929, vol. 16.

the cell as indicators for the penetration of foreign substances. Thus it has been found that caffeine causes a granulation of the myoplasm, and this has been used to test the speed of penetration of caffeine and allied substances into the muscle cells of various amphibia. In some plant cells there are pigments that change color at various hydrogen ion concentrations, and this has been used to test the penetration of various acids and bases.

Of the indirect methods of testing cellular permeability, that which has had the greatest use rests on the osmotic swelling or shrinkage of the cell when placed in a foreign environment. The typical experiment consists in transferring the cell to a foreign solution the osmotic pressure of which is equal to that of the normal environment of the cell, but in which some foreign substance has been substituted for one of the constituents of the cell's normal environment. If this new substance penetrates into the cell more freely than the one for which it has been substituted, the osmotic pressure within the cell will increase in relation to the environment, and the cell will swell by imbibition of water. On the other hand, if the foreign substance penetrates into the cell less freely than the substance for which it has been substituted, the cell will shrink. The shrinkage or swelling of the cell can be observed in some plant cells directly through the appearance or disappearance of a water clear zone between the cell protoplasm and its membrane; in other instances, this may be determined by changes in volume, changes in weight or changes in freezing point or conductivity of the cell protoplasm. This method may be varied by changing the concentration of the test substance, and discovering the time and concentration required to make plasmolysis appear or disappear. It is important in all such investigations that the test solution should not depart so widely from the normal environment as to cause an injury to the cell.

A third method for the determination of cellular permeability rests on the production of physiologic effects by the test substance. This method has been used particularly in studies on parthenogenesis of the eggs of lower organisms. Substances capable of producing parthenogenesis are considered as having penetrated into the interior of the cell.

Whenever the cell or tissue to be examined is found to exist in the form of a membrane, the permeability of the whole membrane may be tested by more simple methods, and quantitative results can be obtained by measuring the amount of test substance which traverses a unit of area of the membrane in a unit of time, when the diffusion pressure or concentration of the test substance differs by unitary amounts on the two sides of the membrane. A further development of this technic consists in measuring the relative proportions in which two substances

diffuse across the membrane, when one of the substances permeates freely, the other being more or less retarded. For highly impermeable membranes, a further refinement has been devised based on the fact that the diffusion velocities of potassium and chloride ions are practically equal. Solutions of tenth-molar and hundredth-molar concentrations of potassium chloride are placed on either side of the membrane. If the membrane impedes the passage of one of these ions more than the other, a measurable difference in electrical potential can be found between the two solutions.

SUMMARY OF FINDINGS

The results of many different workers, who have experimented with a great variety of different kinds of animal and plant cells and with a great variety of different test substances, are difficult to coordinate into any general rules. Taking, however, only the major points of agreement, and discounting the numerous exceptions, the following general rules can be formulated. Among the cations, the following order of decreasing permeability usually holds:

$$NH_3 > K > Na > Ca > Mg$$

while among the anions:

$$NO_3 > Cl > \text{Acetate} > \text{Tartrate} > SO_4$$

In general, anions pass cell boundaries more freely than cations.

The permeability of cell membranes for organic substances that can be arranged in simple series of increasing molecular size decreases with the increasing size of the test substance. In general, the permeation of lipoid-soluble substances is greater than that of equally large molecules of nonlipoid-soluble substance. Mention should also be made of the studies on the penetration of various gases into cells. The rate of penetration for oxygen and nitrogen is usually said to equal that of the same gases through protein solutions and jells; carbon dioxide and hydrogen sulphide appear to diffuse as undissociated molecules.

Cellular permeability is little affected by variation of temperatures which are within physiologic limits, but may be increased by exposure to light and ultraviolet or roentgen radiation. Increase in osmotic pressure of the environment in general causes an increased permeability. The various ions enumerated tend to increase or decrease permeability of cell membranes more or less in proportion to their own rates of permeation. It is interesting to note that normal permeability of cells is best maintained in equilibrated solutions, that is, in solutions similar to sea water for cells which normally live in sea water, and solutions similar to Ringer's solution for the cells of animals with circulating

blood. Changes in p_H of the surrounding mediums result in irregular changes in permeability, which are attributed to: (1) the death of the cell, (2) the change of the membrane potential and (3) the approach of the iso-electric point of the surface proteins. The permeation of alkaloids and other "surface acting substances" is, in general, irregular and not directly related to their molecular size. Great changes in cellular permeability occur during physiologic activity, thus a stimulated cell or one undergoing mitotic division may exhibit a great increase in permeability as compared with a resting cell. On the other hand, the permeability of fertilized ova is generally less than that of unfertilized ova. Injured or dying cells usually show abnormally high permeability.

IRRECIPROCAL PERMEABILITY

When the phenomena of living membranes are investigated, great anomalies in permeability are discovered. Thus, for instance, the frog's skin allows the permeation of water and methylene blue (methylthionine chloride, U.S.P.) much more freely in the direction from outside to inside than in the reverse direction, and a sac made of frog's skin is capable of transferring considerable amounts of water even against an adverse osmotic pressure. Similar anomalies have been found in relation to the intestine, urinary bladder, etc. In general, it may be said that living membranes, bounded on opposite sides by histologically different cell types, exhibit anomalous or "irreciprocal" permeabilities. On the other hand, membranes like the diaphragm, which are bounded on both surfaces by similar cell types are, in general, incapable of exhibiting such anomalies.

The problem of irreciprocal permeability has been the subject of many studies, but its fundamental significance has not yet been explained on a physicochemical basis. Wertheimer [2] has shown that the irreciprocal permeability of the frog's skin is a function of the degree of hydrophilic swelling of the proteins on the opposite surfaces, and that with a change of p_H the swelling of the two surfaces may be affected oppositely, and the direction of the water flow reversed. It is not clear, however, why the hydrophilic tendencies of the two different surfaces do not rapidly attain equilibrium with the surrounding fluid. Unless the equilibrium is constantly being disturbed by virtue of the metabolism of the cells themselves, Wertheimer's hypothesis amounts to a perpetual motion machine. The source of energy required permanently to keep the difference in the hydrophilic potential on the two sides of the frog skin

2. Wertheimer, E.: Weitere Studien über die Permeabilität lebender Membranen, Arch. f. d. ges. Physiol. **201**:591, 1923; Ueber die Quellung, geschichteter Membranen und ihre Beziehung zur Wasserwanderung, ibid. **208**:669, 1925.

has not been discovered. With death of the tissue, the degree of irreciprocity of the permeability decreases, but some vestiges remain for a time even after all other signs of life have disappeared.[3]

CAPILLARY PERMEABILITY

Of special interest to ophthalmologists is the work that has been done on capillary permeability. The literature on this subject is of immense volume since it includes the whole domain of the chemistry of the tissue fluids on the one hand, and the physiology of the capillaries on the other. For an excellent summary of the first of these the reader is referred to the recent monumental work of Peters and Van Slyke.[4] The present status of our knowledge of the physiology of the capillaries may be found in the monographs of Krogh [5] and of Lewis.[6] Clinical studies on the blood, interstitial fluid, etc., have led to the conclusion that the capillary walls behave as inert semipermeable membranes. The chemical constitution of interstitial tissue fluid, lymph, edema fluid, etc. approximates that of a dialysate of the blood plasm. Drinker [7] has recently shown that the capillary walls are not completely impermeable to proteins, and that lymph normally contains from about 1 to 2 per cent of protein derived from the blood. The globulin fraction of the lymph proteins, however, is negligible, and the capillaries, under normal circumstances, may be assumed to be completely impermeable to globulin though slightly permeable to albumin. The percentage of protein in the fluid escaping from the capillaries is probably lower than that in lymph, for water is reabsorbed into the blood stream at the venous end of the capillary, leaving the protein behind, and the latter can only return into the blood by way of the lymphatics. According to Rous,[8] the venous end of the capillaries is more permeable than the arterial end.

The permeability of the capillaries, however, is not a stable, fixed quantity, but varies widely under both physiologic and pathologic conditions, and the results of the studies just referred to are to be interpreted only in relation to the average normal permeability. Under the

3. Amson, K.: Worauf beruht die irreziproke Permeabilität der Froschhaut? Arch. f. d. ges. Physiol. **225**:467, 1930.

4. Peters and Van Slyke: Quantitative Clinical Chemistry, Baltimore, Williams & Wilkins, 1931, vol. 1.

5. Krogh, A.: The Anatomy and Physiology of Capillaries, New Haven, Conn., Yale University Press, 1922.

6. Lewis, Thomas: The Blood Vessels of the Human Skin and Their Responses, London, Shaw & Sons, Ltd., 1927.

7. Drinker, C. K., and Field, M. E.: Protein Content of Mammalian Lymph and the Relation of Lymph to Tissue Fluid, Am. J. Physiol. **97**:32, 1931.

8. Rous, P.; Gilding, H. P., and Smith, F.: The Gradient of Vascular Permeability, J. Exper. Med. **51**:807, 1930.

influence of histamine and other local irritants, capillary dilatation occurs, and with it an increased permeability of the capillary wall. It is not clear whether the increased permeability is directly the result of the capillary distention, or whether the change in capillary permeability and change in capillary tone are independent mechanisms. Both capillary tone and capillary permeability are under the control of the nervous system, possibly through the release of histamine substances in the tissues as the result of antidromic impulses coming down the sensory nerves.[6] It is possible that in some general diseases, such as the nephroses, a generalized increase in capillary permeability may occur.[9]

THE BLOOD-AQUEOUS BARRIER

In the special field of ophthalmology, the studies of various workers on the chemical composition of the aqueous, its osmotic pressure and its conductivity and on the electrical potential difference between blood and aqueous all indicate that the blood-aqueous barrier behaves, on the whole, as an inert semipermeable membrane, and has the general characteristic of capillary endothelium in other organs. This aspect of the subject has been reviewed so frequently in recent years as to require no further comment here (Duke-Elder,[10] Magitot,[11] Sondermann,[12] Yudkin[13]). Numerous studies have been undertaken to investigate changes in permeability of the blood-aqueous barrier under a variety of experimental conditions. Two fairly satisfactory methods exist. On the one hand, the protein content of the aqueous can be measured, and an increase in proteins is taken to indicate an increased permeability of the barrier. On the other hand, the time of appearance in the aqueous of some foreign substance such as fluorescein may be used as an indicator. Thus one can measure the permeability of the blood-aqueous barrier either in terms of the rate of diffusion of some substance to which the barrier is normally permeable, or in terms of the limiting molecular size to which the barrier is permeable. Gaedertz and Witt-

9. Elwyn, H.: Nephritis, New York, The Macmillan Company, 1926, p. 214.

10. Duke-Elder, W. S.: On the Nature of the Intraocular Fluids, Brit. J. Ophth., monograph supp. 3, London, George Pulman and Sons, Ltd., 1927.

11. Magitot, A.: La symptomatologie du glaucome et le problème pathogénique, Ann. d'ocul. **166**:356, 439, 565 and 609, 1929.

12. Sondermann, R.: Beitrag zur Entstehung, Physiologie und Pathologie des Augendrucks, Arch. f. Augenh. **102**:111 and 434, 1930.

13. Yudkin, A. M.: The Aqueous Humor: A Critical and Experimental Study of Its Formation and Chemical Composition, Tr. Am. Ophth. Soc. **26**:319, 1928.

genstein,[14] and more recently Fischer,[15] extended these methods by using a great variety of colloid and crystalloid dyes. In the experiments so far reported, these two methods have given concordant results.

Inorganic acids and bases normally present in the blood, together with related substances, readily make their way into the aqueous. Acid dyes that are highly diffusible, such as fluorescein and eosin, also appear promptly in the aqueous when sufficient amounts have been injected into the blood stream. Some colloids carrying negative charges, such as trypan blue, may also appear in the aqueous, provided they are present in the blood in a high state of dispersion. Diffusible basic dyes, such as methylene blue, do not appear in the aqueous even when injected intravenously in toxic doses. This is to be attributed, not to an impermeability of the blood-aqueous barrier for these substances, but to a binding of these dyes by the proteins of the blood and tissues.

Among the influences that change the permeability of the blood-aqueous barrier are, first, all sorts of local injuries which have recently been exhaustively studied by Poos.[16] He has shown that the intra-ocular vessels, especially those of the ciliary processes, are easily thrown into a state of atonic dilatation, so-called "reactive hyperaemia," analogous to the red reaction which is so readily produced in the skin by simple mechanical stroking. In most instances, this state is accompanied by the presence in the aqueous of vasotoxic substances, evidently released from the injured intra-ocular tissues. These can be demonstrated by injection into the eye of another animal, and are held by Poos to account for the abnormally long persistence of the reactive hyperemia in the eye as compared with other tissues. Lewis [6] expressed the belief that such vasotoxic substances closely resemble histamine, and he has demonstrated their presence in the skin in relation to the red reaction caused by trauma. The work of Poos, then, establishes a close parallelism between the intra-ocular vessels and those of the skin. Just why the H-substances, as Lewis calls these histamine-like substances, so rapidly disappear from the skin after being released by small traumas, but remain in the eye for so long, is not clear. The ease with which such

14. Gaedertz, A., and Wittgenstein, A.: Ueber den Kationengehalt des Kammerwassers im lebenden Warmblüterauge, Arch. f. Ophth. **118**:738, 1927; Untersuchungen über den Stofftransport vom Blut ins Kammerwasser unter besonderen Berücksichtigung physikalisch-chemischer Gesichtspunkte, ibid. **119**:395, 403, 755 and 771, 1928.

15. Fischer, F. P.: Ueber die Permeabilität der Hornhaut und über Vitalfärbungen des vorderen Bulbusaschnittes mit Bemerkungen über die Vitalfärbung des Plexus chorioideus, Arch. f. Augenh. **100-101**:480, 1929.

16. Poos, F.: Ueber die histologischen und klinischen Erscheinungen bei akuten, lokalen Capillarkreislaufstörungen am Auge, Arch. f. Ophth. **127**:489, 1931.

reactive hyperemia can be elicited in the eye is shown by Krause and Yudkin,[17] who reported that the irritation of a dog's eye by ether vapor during anesthesia was sufficient to increase the protein content of the aqueous.

Local insult with reactive hyperemia is not, however, the only means of experimentally changing the permeability of the blood-aqueous barrier. Section of the cervical sympathetic has been shown by many investigators, including most recently Weselkin [18] and Linksz,[19] to lead to similar changes.

The studies so far mentioned deal with the average effect on the whole intra-ocular vascular system so far as it may be considered a part of the blood-aqueous barrier. More detailed investigations show that this barrier does not behave as a unit, and that the ciliary blood-aqueous barrier has quite different properties from that of the iris vessels and of Schlemm's canal. The permeability of the walls of Schlemm's canal was studied long ago by Leber,[20] and more recently by Seidel,[21] who have shown that this part of the blood-aqueous barrier closely resembles capillary endothelium in its behavior. Crystalloids and small sized colloids readily escape from the anterior chamber into the episcleral veins, whereas colloids of large size remain for long periods in the anterior chamber, and their ultimate mode of escape is not precisely known. It may be noted that while Leber and Seidel believed that the foreign crystalloids which they found in the episcleral veins after injection into the anterior chamber reached there through Schlemm's canal, this cannot as yet be regarded as certain. From the experiments so far reported, the escape of crystalloids from the anterior chamber might equally well be assumed to take place, in whole or in part, through the iris vessels.

17. Krause, A. C., and Yudkin, A. M.: The Chemical Composition of the Normal Aqueous Humor of the Dog, J. Biol. Chem. **88**:471, 1930.

18. Weselkin, P. N.: Zur Frage nach Beeinflussung der Permeabilität der Augengefässe durch sympathische Innervation, Ztschr. f. d. ges. exper. Med. **66**: 614, 1929.

19. Linksz, A.: Untersuchungen über den Einfluss des Sympathikus auf die Permeabilität der Augengefässe, Arch. f. Augenh. **104**:264, 1931.

20. Leber, T.: Die Circulations- und Ernährungsverhältnisse des Auges, in Graefe-Saemisch: Handbuch der Gesamten Augenheilkunde, ed. 2, Leipzig, Wilhelm Englemann, 1903, vol. 2, part 2.

21. Seidel, E.: Weitere experimentelle Untersuchungen über die Quelle und den Verlauf der intraokularen Saftströmung, Arch. f. Ophth. **104**:357 and 403; **107**:101, 1921; Ueber den experimentellen Nachweis des Flüssigkeitsabflusses aus der vorderen Augenkammer des lebenden Tieres bei normalen und subnormalen Augendrucke, Klin. Monatsbl. f. Augenh. **68**:291, 1922; Zum Nachweis des Flüssigkeitswechels im Auge, ibid. **69**:773, 1922.

There is histologic and experimental evidence to show that acute glaucoma is accompanied, and perhaps produced, by an acute vascular crisis in the ciliary body, the essential feature of which is an increased permeability of the ciliary capillaries.[22] Magitot [11] assumed that a similar increase in capillary permeability is the cause of chronic simple glaucoma, and Thiel [23] has shown that the blood-aqueous barrier is more permeable to fluorescein in simple glaucoma than in normal eyes.

Recent investigations in relation to the ciliary blood-aqueous barrier have shown that in this special region, phenomena of anomalous and irreciprocal permeability are to be discovered.[24] This barrier is permeable to water in the direction from capillary to intra-ocular cavity, but it resists the transfer of fluid in the opposite direction. The membrane shows the same irreciprocal permeability to methylene blue. Anomalies of this kind were to be expected in view of the complicated and asymmetric histologic structure of this barrier.

PERMEABILITY OF THE CORNEA

The same sort of irreciprocal permeability has been found by Fischer [25] to exist in the cornea. Water and positively charged ions diffuse through the cornea from the external surface toward the aqueous, but not in the opposite direction. Negatively charged ions can diffuse into the cornea from the anterior chamber, but not from the external surface. It seems altogether probable that, in relation to certain ocular diseases, such as relapsing erosion of the cornea and epithelial dystrophy, abnormalities in corneal permeability may play an important rôle. There is some evidence [26] that in acute glaucoma the edema of the cornea may not be due exclusively to the increased intra-ocular pressure, for the edema may be striking in amount in cases with only a moderate increase in intra-ocular pressure, and a similar corneal edema can be produced experimentally by the injection of histamine into the anterior chamber, in which case the intra-ocular pressure is usually subnormal.

Fischer's conclusions are contradicted by Ridley,[27] who has demonstrated that at normal intra-ocular pressure a slow escape of aqueous

22. Friedenwald, J. S.: The Pathogenesis of Acute Glaucoma: I. Clinical and Pathologic Study, Arch. Ophth. **3**:560 (May) 1930.

23. Thiel, R.: Untersuchungen zum Flüssigkeitswechsel am lebenden Menschenauge, Arch. f. Ophth. **113**:347, 1924.

24. Friedenwald, J. S., and Pierce, H. F.: The Circulation of the Aqueous, Preliminary Report, Bull. Johns Hopkins Hosp. **49**:259, 1931.

25. Fischer, F. P.: Untersuchungen über Quellungsvorgänge und über Permeabilitätsverhältnisse der Hornhaut, Arch. f. Augenh. **98**:41, 1928.

26. Friedenwald, J. S., and Pierce, H. F.: The Pathogenesis of Acute Glaucoma: II. Experimental Study, Arch. Ophth. **3**:574 (May) 1930.

27. Ridley, F.: An Experimental Investigation into the Intraocular Pressure and Drainage of the Aqueous Humour, Tr. Ophth. Soc. U. Kingdom **50**:268, 1930.

from the anterior chamber through the cornea may be observed. This is the direction in which Fischer believes the cornea to be normally impermeable to water. It must be noted, however, that Ridley's experiments were performed on dead eyes, and that the concept of irreciprocal permeability is intimately bound up with vital activity.

Fischer [28] has studied, also, the permeability of the cornea to alkaloids, a subject on which considerable older literature had already accumulated. It may be noted that, since most alkaloids are surface-acting substances, their penetration into tissues often exhibits great anomalies, and general rules are difficult to formulate. Mention should also be made of the work of Girard, Mestrezat and Morax,[29] who studied the penetration of inorganic ions from the conjunctival sac into the anterior chamber.

PERMEABILITY OF THE LENS CAPSULE

Studies on the permeability of the lens capsule [30] have shown that this membrane behaves as an inert semipermeable barrier, and that it is permeable to water and dissolved substances, including medium sized colloids, but is impermeable to large colloids. Its general level of permeability is, therefore, similar to that of the capillary endothelium. I have found that the permeability of this membrane decreases with age, and that the decrease in permeability is capable of producing cataracts. Löwenstein,[31] on the basis of his experiments, expressed the belief that just the contrary is true.[31a]

The permeability of the lens capsule must not be confused with that of the lens fibers. Here are cellular structures surrounded by what appears to be a lipoid membrane presenting some analogies to that of red blood cells. Like the red blood cells, the lens fibers largely lack nuclei, and their metabolic requirements appear to be correspondingly low. The analogy should not, of course, be pressed too far, but in the absence of any direct experimental evidence one would expect the lens

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28. Fischer, F. P.: Ueber die Durchlässigkeit der Hornhaut für Alkaloide, Arch. f. Augenh. **104**:121, 1931.

29. Girard, Mestrezat and Morax: Recherches expérimentales sur la permeabilité des tissus vivants aux ions, Compt. rend. Soc. de biol. **87**:69, 1922; Recherches expérimentales sur la permeabilité cellulaire aux ions, ibid. **87**:227, 1922.

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31. Löwenstein, A.: Eine neue Anschauung über die Entstehung des Alterstars, Arch. f. Ophth. **116**:438, 1926.

31a. Since this paper was submitted for publication, Gifford, Lebensohn and Puntenny have reported experiments confirming mine (Biochemistry of the Lens: Permeability of the Capsule of the Lens; this issue, p. 414).

fibers to show anomalies of permeability similar to those of red blood cells—a suspicion supported by the diabetic change in refraction as interpreted by Duke-Elder.[32]

PERMEABILITY OF VITREOUS, RETINA AND CHOROID

The permeability of the anterior hyaloid membrane has been discussed occasionally in relation to the pathogenesis of glaucoma (Verhoeff [33]), but has not been subjected to systematic investigation. The barrier between vitreous and retina is apparently permeable (in the direction from vitreous to retina) to dextrose (Adler [34]) and to potassium ferrocyanide and iron ammonium citrate (Evans [35]), but not readily so to water. The difficulties in squeezing water from the vitreous into the retina may, however, be mechanical and not dependent on an impermeability of the boundary. In albuminuric retinitis, and in various intra-ocular inflammatory diseases, it is apparent that this barrier is permeable to proteins in the direction from retina to vitreous.

Since the rods and cones depend for so large a portion of their nutrition on the choroidal capillaries, some knowledge of the permeability of Bruch's membrane and the retinal pigment epithelium would be most desirable. As yet no studies have been made in this field, but it is to be hoped that the current revival of interest in the pathogenesis of retinal detachment may lead to investigations of this subject.

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32. Duke-Elder, W. S.: Changes in Refraction in Diabetes Mellitus, Brit. J. Ophth. **9**:167, 1925.

33. Verhoeff, F. H.: Pathogenesis of Acute Glaucoma, Arch. Ophth. **54**:30, 1925.

34. Adler, F. H.: An Investigation of the Sugar Content of the Ocular Fluids under Normal and Abnormal Conditions, and the Glycolytic Activity of the Tissues of the Eye, Tr. Am. Ophth. Soc. **28**:307, 1930.

35. Evans, J. N.: Retinal Perivascular Delineation, Tr. Am. Ophth. Soc. **29**: 395, 1931.

News and Notes

EDITED BY DR. JOHN HERBERT WAITE

GENERAL NEWS

"Janus Stolp" Competition.—The governors of the "Janus Stolp" foundation in the University of Leiden, at their meeting on May 25, 1932, decided on the following subject for their biennial scientific competition: "An Original Contribution on the Psychology of the Knowledge of Space in the Blind." Observations among the blind in the solution of the problem of their knowledge of space should be capable of being subjected to scientific criticism. The education of blind persons is directed to increasing their power of orienting themselves in space, to enable them to construct objects or to do manual work, to orient themselves in the street or in the house and, more especially, to give them an idea of geometry. Interesting conclusions might be drawn from an analysis of the practical work of blind surveyors and perhaps also from the observation of blind workmen. It is desired that competitors should choose only a part of the subject, but of sufficient extent to enable them to make a general résumé and a critical review. Entirely theoretical disquisitions, as well as observations embracing too many diverse points, are not desirable. The manuscript must not exceed 40,000 words, and should be sent to the President of the Board, M. le professeur Dr. W. S. Kristensen, 31, Witte Singel, Leiden, before Jan. 1, 1934. It must be typewritten in Dutch, German, English, French or Latin, signed with a motto and accompanied by a sealed letter bearing the same motto and enclosing the name and address of the author. The winning competitor will receive a gold medal of the value of 250 florins and 250 florins in money, or, if he should prefer it, the whole sum in money.

Residency in Ophthalmology.—A residency in ophthalmology with stipend is available at the University of Oregon Medical School. Details concerning the qualifications and duties may be obtained by addressing the dean of the school, Dr. Richard B. Dillehunt, Portland, Ore.

SOCIETY NEWS

American Academy of Ophthalmology and Otolaryngology.—The thirty-seventh annual meeting of the Academy will be held in Montreal, Canada, Sept. 19 to 23, 1932, at the Mount Royal Hotel. The president is Dr. S. Hanford McKee, Montreal; the president-elect, Dr. Burt R. Shurly, Detroit, and the secretary-treasurer, Dr. William P. Wherry, Omaha. On Saturday, September 17, will be held the examinations of the Board of Otolaryngology and the annual golf tournament (Mount Royal Golf Club); on Monday, September 19, the examinations of the (American) Board of Ophthalmic Examiners. On Tuesday, September 20, at 9 a. m., a symposium on "The Progress of General Medicine in Relation to Diseases of the Eye, Ear, Nose and Throat" will be pre-

sented. Section meetings will be held in the afternoon on September 20, 21, 22 and 23. The instructional program will consist of 158 conferences under the guidance of 65 instructors. Demonstrations will be held Wednesday, Thursday and Friday mornings. There will be four special courses: "Histopathology of the Eye," "Histopathology of the Nose, Throat and Ear," "Lesions of the Fundus" and "Clinical Pathology of Otitic Lesions." The instructional program offers the members of the society unusual opportunities in postgraduate work. Special research demonstrations will be made by the Research Fellow for Ophthalmology, Dr. Daniel V. Kirby, and the Research Fellow for Otolaryngology, Dr. William J. McNally. At the Teachers' Section Dinner a report will be made on the present methods of undergraduate teaching of ophthalmology and otolaryngology. The visiting ladies will be entertained by golf, tennis and boat trips and in many other attractive ways.

Pacific Coast Oto-Ophthalmological Society.—At a meeting of the Society held in Seattle on June 30, Dr. Hans Barkan of San Francisco was elected president, Drs. Bertram C. Davies of Los Angeles and Leo B. Bouvy of La Grande, Oregon, vice presidents and Dr. J. Frank Friesen of Los Angeles secretary.

Correspondence

HOMATROPINE CYCLOPLEGIA

June 17, 1932.

To the Editor.—In regard to Dr. Linn Emerson's letter in the June ARCHIVES (7: 954, 1932), I wish to state that I have used for years one-fifth grain (13 mg.) of homatropine dissolved in 4 drops of boiled hot water; 1 drop of this is instilled in each eye, followed in ten or fifteen minutes by the remaining drop in each eye. In half an hour after the last drop, refraction and retinoscopy are very satisfactory. I have repeatedly added atropine afterward to get further cycloplegia, but without much result. There is no pain following the drops.

The use of homatropine as described, followed by a drop of physostigmine solution, allows the patient to become practically normal in six hours. I should like others to try it. I have never seen any ill result.

NORMAN W. PRICE, M.D., Niagara Falls, N. Y.

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Anatomy and Embryology

THE ZONULE IN VERTEBRATES. M. TEULIÈRES and J. BEAUVIEUX, Arch. d'opht. **48:** 465 (July) 1931.

In order to determine from an anatomic point of view whether the zonule has the double function of a suspensory and accommodative ligament in various classes of vertebrates, as has been demonstrated in man, the authors have systematically examined this structure in a large number of vertebrates. Illustrations depict the character of the zonule in most instances in addition to a careful description. The interpretation of anatomic studies is considered under the subheadings of (*a*) the suspensory function of the zonule and (*b*) the part played by the zonule in accommodation.

There is no doubt but that the lens is held in the patellar fossa of the vitreous by the zonule, but the arrangement of the zonular fibers varies in the different classes of vertebrates. In fishes, it has a triangular or quadrilateral form situated at the upper part of the lens. In all other classes, it is perilenticular. Sometimes it is fan-shaped, harp-shaped or triangular with a group of reinforcing fibers anteriorly, sometimes spread out or separated into anterior and posterior fibers to form a cavity between them. Great variation occurs also in the direction taken by the fibers. The zonule is always independent of the vitreous, and its fibers are much stronger as the volume of the lens increases.

As for the part the zonule plays in the act of accommodation, from an anatomic standpoint it is easy to say that the zonule has no accommodative function in fishes. In reptiles and batrachians the zonule seems to have no action because of the narrow space between the equatorial crest of the lens and the ciliary processes. In some birds relaxation of the zonule may play a part in accommodation. In mammals these anatomic studies lead the authors to believe that the theories of Helmholtz and Tchering are insufficient to explain accommodation in them. They call attention to the insertion of the zonular fibers to the equator of the lens and its immediate neighborhood. On the other hand, in monkeys the zonular fibers play an active part in accommodation whatever theory is admitted. The same is true in man. Moreover, the widespread attachment of the zonular fibers to both surfaces of the lens as well as to its edge makes its accommodative function more powerful.

S. B. MARLOW.

Bacteriology and Serology

THE BLOOD PRECIPITATION TEST IN OPHTHALMOLOGY. WACHENDORFF, Klin. Monatsbl. f. Augenh. **86:** 648 (May) 1931.

Referring to the research of Pavkovits-Bugarszky on the blood precipitation reaction (Valuation of the Rapidity of the Precipitation of the Red Blood Corpuscles in Diseases of the Eye, *Klin. Monatsbl. f. Augenh.* **85:** 528 [Oct.] 1930; abstr., ARCH. OPHTH. **6:** 284 [Aug.] 1931), the author reports the results he obtained with the method of Westergreen in 1926. As in the aforenamed studies, he frequently found no acceleration of the settling time in glaucoma, which in his opinion was due in these cases to arteriosclerosis, rather than to glaucoma. The reaction is valuable in distinguishing benign and malignant cases of ocular tuberculosis, the settling time being decidedly shorter in malignant and stubborn cases. Wachendorff used this test to avoid possible overdoses when treating with tuberculin. Two cases are mentioned of patients with disturbances of the optic nerves. They reacted to the first injection of tuberculin so violently that the treatment was temporarily discontinued. A few days later the settling time had decreased, whereupon further injections were considered safe and were actually followed by the desired result. Contrary to Pavkovits, Wachendorff found that rapid precipitation in iridocyclitis does not indicate rheumatic origin and exclude syphilis. He refers to a publication on rapid precipitation and negative Wassermann reactions in cases of advanced syphilis. These patients require antisyphilitic treatment. Rapid precipitation in iritis and purulent conditions may actually help to clear up the diagnosis in syphilis.

K. L. STOLL.

Conjunctiva

BIOMICROSCOPY IN A CASE OF CONJUNCTIVAL TUBERCULOSIS. CUÉNOD and NATAF, Arch. d'opht. **48:** 541 (Aug.) 1931.

This report is a contribution to the differential diagnosis between trachoma and tuberculosis of the conjunctiva. The authors describe a case of proved tuberculosis of the conjunctiva which they observed over a period of several months with the corneal microscope. Although tuberculosis of the conjunctiva is not uncommon, many cases being described in the literature, in regions in which trachoma is prevalent tuberculosis of the conjunctiva may be mistaken for trachoma, or overlooked. The conjunctiva of the upper lid is the part to be examined, as that of the lower lid is too lax. Whereas in trachoma the projecting follicles or papules are seen, tuberculosis begins as small depressed points of necrosis, which gradually become surrounded by a ring of follicles, to form a round, swollen mass with an umbilicated center. Well formed tuberculous follicles are much larger than those of trachoma.

S. B. MARLOW.

Experimental Pathology

ACTION OF SOME DERIVATIVES OF CHOLINE ON THE NORMAL AND THE PATHOLOGIC EYE. V. ROSSI, Arch. di ottal. **38:** 573 (Nov.) 1931.

The author reviews recent reports on the use of acetylcholine and acetylcholine hydrochloride in spasm of the central artery and other conditions and his own work on an extract of lymph nodes, which caused a decrease of intra-ocular tension. His present work reports observations on eyes treated with acetylcholine hydrochloride. Instillation was without effect on the tension of normal rabbits' and human eyes. A decrease of from 3 to 4 mm. followed subconjunctival injection, but this did not last longer than one hour. Injection of from 2 to 3 drops of 5 per cent solution into the vitreous caused severe inflammation with lowering of tension for two hours. It also promoted the passage of sodium fluorescein given by vein or subcutaneously into the aqueous. The subcutaneous injection of epinephrine retarded this process. In a small group of cases of absolute glaucoma injection of acetylcholine hydrochloride into the vitreous was without effect on the tension, but caused severe pain and inflammatory symptoms. Thus its effect on tension would seem to depend on the presence of normally reacting vessels.

S. R. GIFFORD.

EXPERIMENTS ON THE ACTION OF THE ROENTGEN RAYS ON RABBITS' EYES. R. AULAMO, Klin. Monatsbl. f. Augenh. **86:** 473 (April) 1931.

The left eyes of nineteen rabbits were exposed to roentgen rays of varying strength and quality, and were then histologically examined. The soft rays were filtered through an aluminum filter of 1 mm. thickness and a spark distance of 25 cm. was used for exposure. The hard rays were applied at a spark distance of 46 cm. after passing through a copper filter of 0.5 mm. thickness. The dose was measured by the Holzknecht method in each case. The effect of soft and hard rays was nearly identical; the soft ones seemed to affect the eyes slightly more. The skin erythema dose was the smallest to produce an effect. Shrinking and atrophy of the conjunctiva, as well as opacification of the cornea in the area of the palpebral fissure only, were observed. Soft and hard rays produced a cataract which began at the posterior portion of the lens, similar to a choroidal cataract. Total opacification soon followed. Very small doses, which produce no visible changes, may still cause a cataract. Microscopic examination showed the lens capsule intact, while the nucleus was totally destroyed. Changes of the choroid and ciliary body could not be noticed histologically, owing, perhaps, to the paraffin method which was employed. Hypertrophy of the walls of some ciliary vessels may have been of a pathologic nature.

K. L. STOLL.

General

QUALITATIVE INORGANIC ANALYSES OF THE SCLERA IN NORMAL HUMAN EYES. J. STREBEL, Schweiz. med. Wchnschr. **61:** 1102 (Nov. 14) 1931.

A preliminary report is made of a work which will seek to investigate the qualitative analysis and comparison of the composition of normal and highly myopic eyes. The aims of the investigation were set forth in 1913 in the eighty-fourth number of Deutschmann's *"Beiträge zur Augenheilkunde."* It is essentially a contribution to the problem of myopia. The author's basis for the chemical investigation is rationalized on several factors which point to a change in the make-up of the sclera, which may be due in part to physicochemical relations. He refers to the work of A. Steiger and Professor Sidler, who seem to have shown that the pull of the external muscles in the act of convergence has a decided effect on the posterior pole of the sclera. This may account for the fact that the conus, the staphyloma vera and the macular degeneration together with scleral thinning are diseases of the temporal portion of the globe. In a previous work the author has shown that the empiric use of magnesium, phosphorus and calcium compounds, together with full correction of the myopia and decrease of converging and accommodation movements, has tended to prevent the progress of the myopia. A detailed chemical method is outlined with the help of the chemist of the University of Zurich. The author concludes that the normal human sclera is rich in calcium and magnesium phosphates. The author believes that only by the analysis of all the complex and multitudinous factors of the problem of myopia will progress be made.

L. L. MAYER.

Lacrimal Apparatus

A GRAVE LATE COMPLICATION OF DACRYOCYSTORHINOSTOMY. M. MARÍN-AMAT, Arch. d'opht. **48:** 632 (Sept.) 1931.

Because of his experience with the two cases described in this report, the author believes that dacryocystorhinostomy can no longer be considered free from danger but should be looked on as a serious operation as life may be endangered by it. Preliminary to it, the bleeding time and clotting time of the blood as well as the patient's nose should be thoroughly investigated. The two cases described occurred in a series of 250 operations done during a period of five years. In both, five days after the operation, a severe hemorrhage from the nose and mouth occurred, which could not be controlled by any of the usual methods of packing the nose and nasopharynx or by internal medication. In the first case the bleeding spontaneously stopped at the end of four days, leaving the patient extremely anemic. The second case was more severe, apparently an arterial hemorrhage. Transfusion became necessary to keep the patient alive, and the hemorrhage was checked only after the exposure of the lateral wall of the nose and the direct application of pressure to a bleeding artery.

S. B. MARLOW.

Lens

CLINICAL AND EXPERIMENTAL STUDY OF WOUNDS IN THE CAPSULE AND POSTERIOR LAYERS OF THE LENS. G. SANNA, Ann. di ottal. e clin. ocul. **59:** 543 (June) 1931.

The author reports two cases in which the posterior lens capsule was wounded. In the first, a small piece of steel passed through the cornea and iris 2 mm. from the limbus. The lens showed a posterior stellate opacity one ray of which was continuous with a small opacity at the equator, the rest of the lens being perfectly clear. The foreign body was localized near the posterior pole, and a large hemorrhage could be seen covering the disk. The opacity cleared slowly, and two months later formed a sharply outlined oval opacity from the central region to the equatorial opacity previously noted. A year later this was further reduced in size and presented a spongy appearance with areas of clear lens in the interstices. The second case sustained a penetrating injury to the sclera at the equator. A horizontal break in the posterior capsule 2 mm. long was seen, surrounded by a stellate opacity of the posterior cortex. The opacity remained stationary for two weeks, after which it progressed until, after one and a half months, the whole lens was opaque.

A number of similar cases from the literature are reviewed, with the attempts of several authors to explain the formation of the stellate opacity without direct injury to the posterior cortex. Results of previous experimental work, which is reviewed, agree that while wounds in the anterior capsule or equator of animals close by proliferation of the capsular epithelium, wounds in the posterior capsule give rise first to globules of degenerated lens tissue which are replaced by connective tissue.

The author wounded the lens of rabbits in various ways and observed the resulting changes in the lens after incisions of the capsule alone; the wound was seen to become wider during successive days, but the cortex remained clear during an observation of months. When a deeper incision was made involving some cortex, the cortex remained clear for several days, but swelled and bulged through the wound, forming a picture of posterior lenticonus. The lens usually remained clear, except in a few cases in which a circumscribed opacity occurred. In only one case did this progress to involve the whole lens, and in this case considerable trauma was inflicted on the lens fibers. In one case in which a puncture was made through the entire lens, the anterior wound closed rapidly without the production of opacity, while the posterior wound remained open with typical lenticonus. Lenticonus never occurred when the anterior capsule alone was incised.

The difference in behavior of anterior and posterior capsules, according to the author, is because of the absence of epithelium in the posterior capsule. The absence of the capsule, however, does not cause opacity of the lens unless the fibers are broken down. Some damage to the interfibrillar cement substance evidently occurs when the capsule is broken,

but opacities so produced clear in the rabbit lens unless the fibers are broken down.

The author believes that the capsular epithelium acts to cover wounds of the anterior capsule and so prevents mechanically a contact with the aqueous without having any selective filtering effect. A bibliography accompanies the article.

S. R. GIFFORD.

THE HISTOLOGY OF THE DETACHMENT OF THE ANTERIOR CAPSULAR LAMELLA OF THE CATARACTS OF BLACKSMITHS AND GLASS-BLOWERS ("HEAT DETACHMENT," OR SOLUTIO LAMINAE CAPSULAE ANTERIORIS). A. VOGT, Klin. Monatsbl. f. Augenh. **86:** 736 (June) 1931.

The author extracted red cataracts in two men, one a glass-blower, aged 65, the other a blacksmith, aged 76. In both cases nuclear and posterior cortical cataracts were present and, also, detachments of the lamella of the anterior capsule. Before delivering the lenses, Vogt removed large pieces of the anterior capsule with well opened de Wecker's scissors. The pieces were embedded in paraffin and showed in each case the detached lamella, which involved about one half of the total thickness of the capsule. This thickness varied and was wavy in one series of cuts, due to reattachment, being generally far thicker than the senile exfoliation of the capsule. This would explain the clinical difference between these two types, for instance, the continuity of the lamella in furnace workers, which rises up and down in the aqueous, presenting a tough and elastic aspect. The senile exfoliated capsule, on the other hand, is thinner and floats in the aqueous, showing a tendency to disintegrate.

It is impossible to ascertain the cause of the damage in the eyes of fire workers, although the intense striation of the lamellae seems to indicate that certain lamellae and their connecting substance (Kittsubstanz) were damaged by radiation and convective heat.

Vogt distinguishes between the two mentioned types and the detachment of the zonula. He stresses the point that none of these three types is ever found in combination with either of the others.

K. L. STOLL.

Lids

A CASE OF SODOKU OF THE LIDS. MONTHUS, FAVORY and LEVADITI, Arch. d. opht. **48:** 493 (July) 1931.

The case of a child, 1 year old, with a rat-bite of the lid is reported. No organisms were found after a careful search. Death occurred notwithstanding the prolonged use of arsenicals. The fatal outcome of this case the authors attribute to the location of the initial lesions and the poor resistance of the patient. The characteristic clinical picture of sodoku includes an incubation period of from fifteen to twenty days (reduced to five or six in the severe cases). A more or less tender red swelling occurs at the site of the bite. When this swelling is incised, only a serosanguineous fluid escapes. Neighboring lymph glands are swollen. The temperature is elevated, but subsides when the localized swelling

diminishes. General symptoms may appear which sometimes resemble measles. The disease lasts from two to three months before cure ensues. The mortality is between 6 and 12 per cent. The infective organism, a spirillum, is rarely found in the blood. The Wassermann reaction is almost always positive, and arsenical treatment usually beneficial.

Sodoku of the lid is very rare, the lower extremities and hands being the common sites of the initial lesion.

S. B. MARLOW.

Neurology

OPTIC ATROPHY DUE TO HYPOPHYSEAL DISEASE. W. MEISNER, Deutsche med. Wchnschr. **57**: 1368 (Aug. 1) 1931.

CASE 1.—A man, aged 40, noticed spots before his left eye in 1919. The history included a mild case of malaria and a negative Wassermann reaction. The visual acuity in the right eye was 5/5; that in the left eye, 5/3, with a paracentral, temporal, relative scotoma for red in both eyes. The fundi showed "drusen," near the macula in the right eye, with a small degree of temporal pallor of the left disk. In spite of abstinence from coffee and nicotine, the visual acuity was reduced to 5/50 or 5/30 in the left eye in 1922. When the patient was seen by the author one month later, there was a bilateral hemianopia for red in the temporal region and the upper quadrant. There was only a relative scotoma for white. Roentgen examination of the sella at this time showed a typical widening, establishing the diagnosis. Roentgen therapy was instituted, and at the last examination in 1930 there was no change in the visual fields, and the acuity was 5/7 in the right and 5/50 in the left eye.

CASE 2.—A man, aged 51, had been treated for two years by various physicians for bilateral optic atrophy. In spite of a negative Wassermann reaction of the blood and spinal fluid, he was thought to have tabes and was treated with arsphenamine. Examination by the author showed a visual acuity of 5/18 for the right eye, corrected to 5/8 with a compound myopic lens. The left eye had perception only for hand motion, eccentrically in the nasal field. There was a complete right temporal hemianopia for red. For white, there was only a relative paracentral scotoma in the lower quadrant temporally. Neurologic examination revealed "a not entirely outspoken but probable picture of dystrophy adiposogenitalis, as the x-ray picture showed a broad sella." However, roentgen therapy of the hypophysis had checked any advance in the condition. The author makes a plea for the use of the fields for color in this type of case.

L. L. MAYER.

Ocular Muscles

CONGENITAL BILATERAL PARALYSIS OF THE LATERAL MOVEMENTS OF THE EYES. A. COLRAT, Arch. d'opht. **48**: 822 (Dec.) 1931.

The author describes the case of a little girl, 2½ years old, brought to him by her parents because she could look neither to the right nor to the left. The parents were first cousins, the patient being the fifth of six children; the two oldest were dead. The patient was a full-time healthy

baby but did not learn to walk until 20 months old. Her eyes were almost fixed in the beginning with an internal strabismus more marked than at the time of examination. Gradually the vertical movements developed, so that elevation and depression were almost normal when examined. Convergence was somewhat defective, but present, and was accompanied by constriction of the pupil, although this reaction was not so good as that to light. The right eye turned in about 5 degrees. Voluntary movements of either eye to the right or left were completely absent. Rotation of the head also showed passive lateral movements absent. There was no ptosis or facial paralysis. Similar cases have been reported by Jacqueau, Fryer and Sauvineau. No completely satisfactory explanation is known, but the hypothesis of a lesion involving the sixth nuclei or the fibers running between them and the posterior longitudinal bundle is attractive.

S. B. MARLOW.

Orbit, Eyeball and Accessory Sinuses

CHLOROMA OF THE ORBIT: REPORT OF A CASE. N. BLATT, Klin. Monatsbl. f. Augenh. **87**: 209 (Aug.) 1931.

A survey of the ophthalmologic literature, compiled by Blatt, showed the extreme rarity of chloroma of the orbit and the uncertainty of its origin. Some authors consider it a biologic variety of leukemia, others a tumor related to sarcoma. The author's case concerns a girl, aged 3, with exophthalmos of the right eye in a completely fixed position. The lids could not be closed, the pupils were large and rigid, the disk was pale, and the retinal vessels were normal. Hard and uneven tumor masses could be felt above and below the globe. The left eye was found outside the lids and embedded in brownish-green tumor masses, the size of a hen's egg, which also protruded and showed an uneven surface, partly bleeding and gangrenous. Other tumors could be palpated on the temples and at the border of the scalp on the forehead; smaller nodules were disseminated in the scalp and apparently adherent to the bone. The child was well developed, but either somnolent or excited. Roentgenograms showed an enlarged skull, dilated fissures, periosteal bony formations on the frontal bone and destructions in the sphenoidal, ethmoidal and left zygomatic bones.

The condition of the blood gave no evidence of leukemia. Blatt agrees with Schmaus, who defined chloroma as "round cell sarcoma of the bones, especially of the skull, which contain lipochrome, causing the greenish discoloration." It occurs in persons with an inferior hemopoietic system, based on their embryonic development.

K. L. STOLL.

Pharmacology

THE EFFECT OF ADRENALIN ON THE INTRA-OCULAR PRESSURE AND ITS CHEMICAL SIGNIFICANCE. W. S. DUKE-ELDER, P. M. DUKE-ELDER and J. C. COLLE, Brit. J. Ophth. **16**: 87 (Feb.) 1932.

The experimental methods and results are described, and the following conclusions are drawn:

It appears, as judged from pressure records in the intact animal and the artificially perfused eye, from the change of blood flow as recorded

by temperature changes and from the direct observation of the intra-ocular vessels, that the action of epinephrine on the eye itself, uncomplicated by the effects of the general circulation, is fourfold: First, in small doses it dilates the capillaries and raises the intra-ocular pressure; second, in large doses it constricts the arteries and capillaries and lowers the pressure; third, in any dose it constricts the plain muscle of the orbit and raises the pressure, and fourth, it dilates the pupil, an action which appears to be without any significant influence on the intra-ocular pressure, since it may be associated with either a rise or a fall. In the intact animal, where the situation is complicated by general vascular changes, the raised blood pressure tends to break through any arteriolar resistance which may be present and cause a rise in the intra-ocular pressure unless (with individual variations) the dosage is very high, when (sic.) local constriction of the arterioles may be sufficient to counterbalance this.

In man, the action of Müller's muscle in raising the intra-ocular pressure will be very much less than in the dog, owing to its very small development in the former; it is probable indeed that it may be neglected altogether. Apart from this, the present investigation accounts for the variability of the action of epinephrine on the pressure of the eye. Depending on the dose in which it becomes effective in the eye, it will either dilate the minute vessels, raising the pressure, or constrict them, tending to lower the pressure, and the possibility of the constriction becoming effective will depend on the extent to which the drug is absorbed into the general circulation. The fact that the vessels of the eye react less markedly than those of large areas elsewhere in the body (particularly in the skin, and in the heart itself) makes ocular changes subservient to general changes. A further complication arises which can only be referred to briefly at present. After the minute vessels have been exposed to the action of histamine-like substances, they undergo a refractory phase wherein epinephrine is without constrictive effect. How far this may account not only for the frequent failure of epinephrine to produce a hypotensive effect in cases of acute glaucoma, but also for the fact that it may raise the pressure still further, will be made the subject of a future communication.

W. ZENTMAYER.

Physiology

A METHOD FOR STUDYING THE EXTRAVISCERAL EYE (EXPERIMENT ON HEART-LUNG-HEAD PREPARATION). W. WEGNER and H. F. ROESE, Klin. Wchnschr. **46:** 2133 (Nov. 14) 1931.

The difficulty in making a physiologic or pharmacologic study of the eye as separated from the remainder of the body has been the influence of the organs of internal secretion. The Russian authorities have not been able to control vascular reactions due to the influence of vasomotor substances carried in the defibrinated blood. In spite of the fact that Duke-Elder used an artificial lung in his work, edema and protrusion of the globe were noted. The authors have found that by using the heart-lung preparation of Starling these pressor substances are eliminated from the defibrinated blood as it passes through the lung. In detail, their method is simple. Weese's pump is joined to the usual Starling heart-lung preparation. Without breaking the circulation, can-

nulas are inserted into the carotid arteries and outer jugular veins. A compression clamp takes care of the vertebrals. Optical registration of the pressure in the vessels is obtained with Samojloff's manometer; 1,500 cu. mm. of narcotic-free, defibrinated blood is used at 35 C. With this method the authors have succeeded in maintaining the corneal reflex, the pupillary reflexes and the intra-ocular tension. The usual drug reactions are easily elicited. A bibliography accompanies the article.

L. L. MAYER.

Refraction and Accommodation

HIGH MYOPIA IN THE FIRST YEARS OF LIFE: REPORT OF SEVENTEEN CASES. M. BARTELS, Klin. Monatsbl. f. Augenh. **86:** 770 (June) 1931.

The term high myopia depends on the number of diopters and the age of the myopic person. Myopia of 3 diopters is considered high in a child, aged 3, but not in an adult. Bartels reports seventeen cases of congenital myopia, ranging from 7 to 23 diopters, in children, aged from 2 to 9 years; one case of myopia of 14 diopters in one eye and emmetropia in the other is included. The majority of the cases had changes in the fundus, e. g., conus, staphyloma, accumulation or rarefaction of the pigment and atrophy of the choroid. Nystagmus was present in three cases, divergent and convergent strabismus in three each and coloboma of the iris and choroid in one case. In some of these children disturbances in the growth of the body or retarded size was noticed, occasionally coupled with unusual mental development. Four cases showed progressive myopia, as far as could be ascertained.

The treatment depends on the etiology of the high myopia. Bartels, rejecting Donders' terms of destructive and nondestructive myopia, prefers the division into two groups: the progressive myopia of adolescence and the pathologic congenital myopia of the first years of life, based on malformation. His seventeen cases belong to the latter group, hence the treatment has to consist chiefly in strengthening the body, and possibly in a hormonal therapy, analogous with the use of thyroid preparations in disturbances of the growth in cretins. It is futile to resort to atropine in these cases, which have hardly any power of accommodation. Pilocarpine should be avoided, or used with care. Bartels observed detachment of the retina in a case of high myopia immediately after instillation of one drop of pilocarpine. Moderate use of the eyes, on the other hand, and proper correction with glasses, are recommended. Puncture of the anterior chamber and anterior or posterior sclerotomy may be considered. The children should attend sight saving schools.

Bartels found heredity in six of his cases and consanguinity in none.

K. L. STOLL.

THE PROBLEM OF ACCOMMODATION AND CHANGES IN REFRACTION. H. CASPARY, Med. Klin. **27:** 1717 (Nov. 20) 1931.

That the lens causes changes in accommodation there is no doubt, but whether this is the entire and only mechanism has become of more importance because of the Bates' method which has gained some promi-

nence. The author had an instrument built to study the Purkinje phenomena, and has already reported on the "Synergie Between Accommodation and Pupil Reaction" (*Arch. f. d. ges. Physiol.* **193:** 225, 1921-1922). From a theoretical standpoint, the recti muscles may cause a change in pressure in the globe or have some effect in moving it forward or backward. This also might change the radius of curvature of the cornea. The incidence of aphakic eyes, which appear to have accommodative powers without refractive correction, is well known. The author ingeniously placed a small lamp in an animal's eye, after forcing the lens into the posterior vitreous. By making pressure on the globe, as would be caused by the recti muscles, he was able to produce an image of the lamp on a white surface, the nearpoint being accentuated by increased pressure on the globe. Conclusions from this experiment are that an accommodation effect is produced, without the lens taking part, but presumably due to ocular musculature influence causing (*a*) change of axis, and (*b*) change of tension inside the globe, and therefore disturbance of the radius of curvature of the cornea. In order to make a clinical test, the author used the aforementioned instrument, an illustration of which accompanies the article. The determinations showed that with muscular movement or tension there was a definite change in the corneal curvature, as estimated by the Purkinje phenomena. He suggests that such changes may also be produced by faradic stimulation of the musculature. In conclusion, the author thinks he has shown that accommodation is not only theoretically but actually possible without the lens being involved. He makes a plea for further investigations of this nature, and warns that methods should not be condemned until proof has shown them worthless. He holds no brief for the Bates' method, but simply presents physiologic proof that its basis may be worthy of further consideration.

L. L. MAYER.

THE PROBLEM OF ACCOMMODATION AND CHANGES OF REFRACTION. (REMARKS CONCERNING THE WORK OF DR. HANS CASPARY). R. GUTZEIT, Med. Klin. **28:** 119 (Jan. 22) 1932.

Caspary's work in a measure gives approbation to the idea of Bates and his school. He reinforces strongly the idea that the eye is adapted for near work by contraction of the ciliary muscle, thus strengthening the curvature of the anterior lens surface, and also that the extra-ocular muscles play an important rôle in changes of refraction, because the eyeball is not a fixed body. Caspary believes that through the tension of the superior, inferior and internal recti muscles when the eye converges the axis of the eye is lengthened, aided by the fanning of other musculature. And, finally, as the tension of the contracting ocular muscles is increased, a shortening of the curvature of the cornea occurs.

According to Caspary, three forms of accommodation are set in order: (1) the previously recorded, scientifically based accommodation of the lens by means of the ciliary muscle, according to Helmholz; (2) the outer or axis accommodation, caused by the extra-ocular muscle; also called photographic accommodation, as the picture screen (the retina) is pushed off from the optical system; (3) the corneal accommo-

dation by shortening of its measure of curvature following the increased tension of the eyeball caused by the contraction of the extra-ocular muscles.

The author believes that the following facts speak against the actual rarity of outer or corneal accommodation, viz.; the entire elimination of accommodation with atropinization although convergence remains; the increased tension of accommodation with physostigmine (eserine), also without convergence, and the isolated accommodation paralysis by damage to the innervation of the ciliary musculature (belladonna and meat poisoning, diphtheria, syphilis). The absence of accommodation in aphakic eyes after cataract operation fails to reveal other than lenticular accommodation. Lens accommodation and convergence are so firmly blended that it is difficult to imagine any other purely mechanical mechanism, which also speaks against Caspary's hypothesis. In convergence the medialis contracts and the lateralis relaxes; the former is pulled away from the globe and the latter lies in a discrete mass on the globe; surely, the superior and inferior muscles, which play so small a part in convergence, can have little effect in pulling back the globe and thus causing a lengthening of the axis of the eyeball.

In other ways the author shows the unscientific and rather psychic effect of the Bates method and emphasizes his belief that it should be condemned.

L. L. MAYER.

Retina and Optic Nerve

RELAPSES AND RECURRENCES OF DETACHMENT OF THE RETINA. GONIN, Arch. d'opht. **48:** 487 (July) 1931.

Although relapses and recurrences have the same etymology, the author gives them a different significance. If after a partial, or what appears to be a complete, reattachment, the same retina is again found detached, the author calls this a relapse and believes it to be due to the persistence of the tear which caused the original detachment. Relapses have been usual up to the introduction of the author's method of thermopuncture, but he does not maintain that this procedure cures all cases. Not only may the tears be too large or too numerous to be closed by one cauterization, but many other obstacles may interfere. Relapse, therefore, should not be a surprise to the operator, but should be foreseen so far as possible and the patient warned of the possibility of their occurrence.

If, after a cure has been established, a detachment takes place in another part of the retina, the author calls this a recurrence. Gonin offers the explanation that the conditions which tend to produce a tear in one part of the retina may also be active in another and thus produce a second detachment. The vitreous plays a most important part in their causation. He cites three cases illustrating his argument. He believes that this differentiation lends further support to his faith in the importance of tears in cases of detachment and also gives a surer foundation on which to base operative results.

Early recurrences indicate roughness or improper operative technic. He does not think late recurrences can be connected with an earlier operation.

S. B. MARLOW.

ALTERATIONS OF THE RETINAL REFLEXES. PAVIA, Arch. d'opht. **48:** 566 (Aug.) 1931.

The author presents in detail the observations made in two cases of retinitis with photographs of the fundus. The two cases are quite similar. In the first he shows that lesions of the choroid, whatever their cause, situated in the macular region, produce by edema slight changes in the thickness of the retina, so changing the mirror reflexes that they can immediately be discovered. In the second case the same phenomena are shown to be caused by lesions outside the macula. The author believes that photography of the fundus must be resorted to in order to study these alterations properly. They are the earliest signs of a retinal or choroidoretinal lesion.

S. B. MARLOW.

Tumors

TELANGIECTODIC GRANULOMA IN THE AREA OF THE CARUNCLE AND THE TEAR SAC. REPORT OF TWO CASES. R. SCHEERER, Klin. Monatsbl. f. Augenh. **86:** 445 (April) 1931.

For about two months, a woman, aged 64, had observed a tumor the size of a small pea in the nasal angle of her eye. It was found to be broadly adherent to the caruncle, but not involving the lacrimal apparatus. An uneventful recovery followed the extirpation. One roentgen treatment was given under proper protection of the globe. These telangiectodic granulomas, although never malign, have the tendency to recur, unless totally removed. No information could be gained regarding the origin of the tumor in this case, which is the first one of its kind published in ophthalmologic literature.

In a second case, that of a woman, aged 52, epiphora and purulent discharge were noticed in one eye for a year. Pneumococci were present in the pus, and the syringing fluid did not pass through the tear sac. The latter was found almost entirely filled with granulomatous masses, containing capillaries of varying thickness of their walls. The lumen of the tear sac was filled with pus, its epithelium being well preserved. Only a few cases of telangiectodic granulomas of the tear sac are known.

K. L. STOLL.

Uvea

ACUTE NONPURULENT DIFFUSE EXUDATIVE CHOROIDITIS (HARADA'S DISEASE). KIYOSADA TAGAMI, Acta Jap. Ophth. Soc., September, 1931, p. 114.

In 1926, Harada published a comprehensive study of a peculiar form of choroiditis which was characterized by clouding; detachment of the retina and a diffuse atrophy of the pigment layer followed recovery from the detachment.

Harada's disease occurs in patients between 30 and 50, of good health, with sudden loss of sight in both eyes, which after from five to six days becomes very marked. Then follow headache, loss of appetite, nausea, vomiting and general malaise. There is no fever. There never is any inflammation of the anterior part of the eye; the light reaction of the pupil is weak, and the first fundus change is a slight neuroretinitis, or a diffuse yellowish opacity of the retina and vitreous. After

two or three weeks the general symptoms disappear as the changes in the posterior half of the eye become more marked; detachment of the retina occurs and extends so that the entire retina seems to be detached right down to the papilla in the form of a funnel. After several weeks the detachment gradually becomes flatter, and after attachment, the fundus again presents the normal pink; the choroidal vessels reappear and irregularly placed pigment spots are noted in the fundus. Vision and light sense, which previously were very much affected, finally become normal.

The author has observed this condition in a patient of 51 years; the diminution of sight became so intense that for a time there was no perception of light, and then the vision rose to 0.2. In the acme of the disease the author aspirated some of the subretinal exudate, and injected it into the eye of a rabbit, producing uveitis. He aspirated some of the vitreous of this rabbit's eye and injected it in turn into the eyes of rabbits up to the third generation, and always succeeded in producing the same uveitis. The examination of the eyes of these experimental animals showed a congestion of the uvea, particularly of the choroid, with a serous and fibrinous exudate, detaching the retina from the underlying choroid, and also the choroid from the sclera. The uvea became infiltrated with lymphocytes and large mononuclear cells. The pigment epithelium degenerated, producing hypertrophy, otherwise the retina showed no changes. The visual cells remained intact. These findings explain the clinical symptoms in Harada's disease. The thickening and opacity of the retina as it occurs in the early stages of Harada's disease can be compared to the congestion and exudation of the choroid in the animal's eyes; the edema involved not only the choroid but also the retina, which too explains the redness and blurring of the disk's margins. The detachment of the retina results from an exudation from the choroid, and as the vitreous body is not involved, the retina recovers. Reduction of vision, contraction of the field and diminution of the light sense are due to a functional disturbance of the pigment epithelium and of the visual cells. It is remarkable that in this disease the retina recovers its function so completely. This is presumably explained by the findings in the experiments, characterized by only slight involvement and degeneration of the retina together with complete preservation of the visual cells. The disease is undoubtedly an exudative rather than a purulent type of inflammation, resembling in part the one that is found in sympathetic ophthalmia, except that the giant cells are absent.

A. KNAPP.

Visual Tracts and Fields

PATHOLOGIC OBSERVATIONS IN A CASE OF BINASAL HEMIANOPIA. M. BAURMANN, Arch. f. Ophth. **126:** 203, 1931.

A woman, aged 34, had had headaches for one year and projectile vomiting and poor vision for eight days. She had bilateral choked disks, with 7 diopters of swelling; vision in the right eye was 0.2; that in the left eye, 0.1. Examination of the visual fields showed: The nasal half of both fields was missing; the temporal halves were somewhat contracted. Autopsy revealed a large soft tumor of the brain, which originated from the corpus callosum and extended into the left hemisphere. The third

and the left lateral ventricles were filled with tumor tissue, which proved to be a very soft, cellular glioma with large ectatic lymph spaces. Each arteria cerebri anterior had produced a groove on the respective optic nerve immediately in front of the chiasm, as has also been found by other authors. Microscopic studies revealed a severe degree of atrophy of the noncrossing fibers; the crossing fibers were also found to be badly damaged. No group of fibers was intact. The peripheral bundles in both optic nerves showed definite rarefaction. This discrepancy between histologic findings and function intra vitam makes the explanation of the mechanism in this case very difficult.

P. C. KRONFELD.

Vitreous

SCINTILLATING OPACITIES OF THE VITREOUS IN THE ANTERIOR CHAMBER. R. GALLENGA, Arch. di ottal. **38**: 398 (July-Aug.) 1931.

A review of the literature on scintillating opacities of the vitreous shows a wide variance in explanation of its pathogenesis. The author's patient, a man of 62, was struck in the right eye by a stone, with resulting dislocation of the lens and prolapse of the vitreous into the anterior chamber. When the media cleared, a mass of snowy opacities was seen in the anterior chamber. The opacities were apparently held together in a jelly-like mass, which was continuous with the anterior vitreous, in which similar snowy opacities could be seen. Secondary glaucoma was present, with vision reduced to perception of hand movements. Vitreous aspirated from the anterior chamber was studied chemically. Tests for cholesterol, tyrosine and albumin gave negative results. Phosphates, chlorides, sodium and calcium were present. The blood cholesterol was considerably increased (230 mg.), while the blood calcium was normal (7.5 mg.). The author concludes that the opacities may have been caused by a precipitation of calcium salts in the vitreous due to changes in its chemical composition and perhaps influenced by contact with the aqueous. (Bibliography.)

S. R. GIFFORD.

Therapeutics

THE TREATMENT FOR SPRING CATARRH: LIGHT AS THE DETERMINING CAUSE OF THE DISEASE. GIAN LUIGI COLOMBO, Ann. d'ocul. **168**: 370 (May) 1931.

The following conclusions are drawn:

Spring catarrh in its initial form is completely and rapidly cured by rigorous protection from light and by the desensibilization to light by suitable drops.

The old forms show a rapid lessening of their manifestations of the recurrent attacks (itchiness, hyperemia, discharge) and proceed slowly to their clinical cure by the same measures.

This treatment is practical and easy. The general treatment is simple: sun baths, glandular therapy and iodine and calcium.

The results obtained show that in predisposed subjects (*vagotoniques*) light is the direct local cause of the disease.

S. HANFORD MCKEE.

EXPERIENCES WITH A MIXED HORMONE EXTRACT (EUPHAKIN). MARIE VON KOETELES, Monatsbl. f. Augenh. **87:** 70 (July) 1931.

A connection between the formation of a senile cataract and endocrine dysfunction has been observed in myotonia, tetany, thymicolymphatic status, after strumectomy and in the course of skin diseases. Siegrist, therefore, gave extracts, and recently, tablets of endocrine glands. The author obtained results similar to those of Siegrist, after treating and controlling seventy-six patients at von Grosz' University Eye Clinic at Budapest for the last two years. A proprietary preparation containing pluriglandular extracts was not administered in phakosclerosis or in advanced cataracts, after its inertness had been previously established in a few cases. The opacities in beginning cataracts remained stationary, but they did not clear up. Most promising were cases with peripheral opacities and vision not less than 5/10 or 5/15. The remedy did not produce any untoward effect; the patients felt generally well, and arteriosclerotic disturbances decreased during the treatment. The short period of observation will not yet permit a definite decision as to whether the formation of a cataract can be permanently prevented, or even retarded.

K. L. STOLL.

THE TREATMENT OF RETINITIS PIGMENTOSA BY AMYL NITRITE AFTER IMRE. M. G. RABINOWITZ, Russk. j. opht. **14:** 225 (Sept.) 1931.

The author considers this to be a preliminary report because the period of observation was from one to two and a half months only. He treated eight patients by amyl nitrite as suggested by Imre. This consisted of daily inhalation of 2 or 3 drops of amyl nitrite, the number of inhalations varying from one to ten. The author modified Imre's method by giving nitroglycerin internally from 3 to 6 drops, for a number of days after the course of treatment by amyl nitrite, as he considered the first remedy not to be as strong and to have a more prolonged action than amyl nitrite.

Redness of the face, due to the dilatation of the blood vessels, slight dizziness and headache for a short time were the only disagreeable symptoms observed. However, the pulse was accelerated and the blood pressure was raised in a few patients; therefore this treatment is contraindicated in patients with high blood pressure.

The central visual acuity was improved in six patients, in one of these from 0.4 to 0.85. The visual fields were enlarged in four patients from 15 to 20 degrees, and the dark adaptation taken by the Birch Hirshfeld adaptometer was improved in four patients. No changes were observed in the fundi.

The effect of both amyl nitrite and nitroglycerin lies in the dilation of the retinal and choroidal vessels, which evidently leads to the improvement of nutrition and function of the retina. The treatment should be applied preferably at the incipient stage of the disease when the intact retinal elements can be saved. Thus the degenerative process may be checked, or at least the inevitable blindness may be postponed.

O. SITCHEVSKA.

Society Transactions

EDITED BY DR. JOHN HERBERT WAITE

NEW YORK ACADEMY OF MEDICINE, SECTION OF OPHTHALMOLOGY

A. B. REESE, M.D., *Secretary*

Feb. 15, 1932

MARK J. SCHOENBERG, M.D., *Chairman*

A CASE OF HEMANGIOMA OF THE ORBIT ARISING PROBABLY FROM THE OPTIC NERVE SHEATH. DR. THOMAS H. JOHNSON.

This is a further report on a case of orbital tumor that was shown before the section two years ago. A woman, 30 years of age, who since August, 1925, had had progressive exophthalmos and visual loss in the right eye, presented the following signs: slowly progressing exophthalmos directed in the axis of the orbit, marked visual loss, edema of the optic nerve head and free movement of the globe with hyperopia.

The patient had repeatedly declined surgical treatment until the sight was lost and the proptosis of the eye deforming. Enucleation with removal of the tumor was performed.

I believe that the tumor had its origin within the nerve sheath and was unique in that respect, as a review of two hundred case reports of intradural tumors of the optic nerve failed to reveal a case of intradural angioma.

DISCUSSION

DR. ALGERNON B. REESE: The tumor occupied a site directly behind the globe within the muscle cone. It was irregularly round and about the size of the globe, or approximately 24 mm. in diameter. The mass pressed against the sclera and flattened it somewhat around the posterior pole. This shortened the anteroposterior diameter of the eyeball and caused an increase in the hyperopia. A Weigert stain has not been made, but from the hematoxylin and eosin preparations the optic nerve apparently shows a moderate degree of atrophy.

Under high power magnification the tumor is seen to have a thin fibrous capsule which is intact around its entire circumference. The tumor proper is composed of large cavernous spaces, which vary in size and shape and are filled with blood. The blood in many places shows coagulation, and in the meshwork of the fibrin are hematogenous pigment granules. This is an indication that there was a stasis of the blood in this tumor, or if not a stasis, at least an abnormally slow circulation. The cavernous spaces are lined with cells that resemble endothelium. Some of the walls of the spaces have media of smooth muscle. The stroma is moderate in amount, and its nuclei and fibers have a parallel course except in some places, where they have a concentric arrangement, forming whorls. In other places the nuclei are sparse, and the inter-

cellular substance is hyaloid in appearance. In the interstices of the stroma can be seen diapedesis of red blood cells and hematogenous pigment granules, some of which are free, and some phagocytosed. This point has some clinical significance, as it has been noted in some angiomas of the orbit that the optic disk shows pigmentation as seen by the ophthalmoscope. This has been shown to be due to the impregnation of the nerve with these pigment granules. The diagnosis is cavernous hemangioma.

DR. ARNOLD KNAPP: I do not know why this hemangioma is supposed to have started inside the optic nerve sheath. The illustrations presented tonight do not demonstrate this. Cavernous hemangiomas in the orbit are common, so why was this not an orbital hemangioma rather than the very unusual form of intradural tumor? I cannot conceive of an intradural tumor pressing on the eyeball to produce hyperopia.

DR. DAVID WEXLER: It would be valuable to note whether the dura of the atrophic nerve contained newly formed blood vessels. If this could be done, especially at a point adjacent to the tumor, it would confirm the impression that the angioma arose from the dural sheath.

DR. THOMAS H. JOHNSON: Dr. Knapp's point as to the proof of an intradural tumor is well taken. The few angiomas that I have removed from the orbit have not been encapsulated and have had fibrous bands connecting them with the other structures of the orbit, and it has been necessary to dissect them out. With the index finger this tumor was easily separated from the surrounding tissues, except from what seemed to be the optic nerve. The gross specimen after removal showed the tumor attached to the globe by the optic nerve and the cut end of the nerve at the posterior pole of the tumor. With a loupe the dura, in the mounted specimen, can be traced from the nerve over the front part of the tumor where it breaks up and is lost. In many of the case reports of intradural tumors hyperopia is mentioned as one of the differential diagnostic signs in favor of that condition.

A CASE OF BILATERAL OPHTHALMOPLEGIA EXTERNA COMPLICATING EXOPHTHALMIC GOITER. DR. THOMAS H. JOHNSON.

A man, 48 years of age, had had a partial thyroidectomy at the Long Island College Hospital in September, 1929. In July, 1930, paralysis of the right inferior rectus muscle developed. By January, 1931, the condition had progressed to exophthalmoplegia externa. The sphincter of the pupil has remained active. The exophthalmometer reading was: right eye, 24; left eye, 25. The basal metabolism was + 28. Thorough study of the patient in the Neurological Institute failed to show a cause for the ophthalmoplegia other than a thyrotoxicosis. I invited the attention of the members of the society to a discussion of this subject by Foster Moore in his "Medical Ophthalmology."

DISCUSSION

DR. JOHN H. DUNNINGTON: The interesting point about this case is the site of the lesion—whether it is the muscles themselves, or whether it is innervational. Most of the cases of muscle paralysis in exophthalmic goiter have been attributed to defects in the muscles themselves, and the opinion is based largely on a few postmortem examinations and on

biopsies. However, that evidence does not seem strong enough to me, particularly in view of the recent operation that Dr. Naffziger did to cure a severe exophthalmos, in which there was no paralysis in any of the extra-ocular muscles; he found the muscles greatly thickened and infiltrated, with destruction of the muscle tissue. So it seems to me that the changes in the case presented here might be a simple accompaniment of the severe exophthalmos rather than the causative factor of the paralysis. In my opinion the lesion is more likely to be innervational than in the muscles themselves.

A Case of von Recklinghausen's Disease Associated with Unilateral Pulsating Exophthalmos. Dr. John M. Wheeler.

I. C., a Jewish girl, aged 16, has ptosis and deformity of the right upper eyelid. There is no significant family history. When the patient appeared on October 14, 1931, she said that the right eye was more prominent than the left at birth, and there was swelling in the region of the temple. The right eyelid always drooped, and vision was never good in that eye. There was considerable thickening of the right upper eyelid, and there was a rim of tissue below the cilia line. In addition there was a deforming notch about the junction of the outer two fourths of the upper eyelid. The thickening extended back over the orbital margin into the region of the temple. Just in front of the right ear there was a large molelike lump. There was easily recognizable pulsation of the right globe synchronous with the radial pulse, but no bruit was present. Over the body were numerous spots of brown pigmentation. There was elephantiasis of the right buttock with a girdle of brown skin. Dr. J. P. Webster has performed two plastic operations for reduction of the enlargement of the buttock.

Dr. L. T. LeWald made a roentgen examination of the head and reported as follows: "Stereoscopic radiographic examinations made of I. C. on Dec. 12, 1931, revealed the following findings: There is an absence of the bony wall at the posterior border of the right orbit. This appearance is practically the same as that observed in the two other patients. In addition to the deficiency in the posterior wall there is also deficiency in the superior and also in the external wall of the right orbit. The sella turcica is unusually deep and large. It measures approximately 2.0 cm. in depth and 1.8 cm. in an anteroposterior direction. A supplemental report will be made after further study of the case."

On November 21 an excision of neoplastic tissue from the lid margin was made. The lid was split and the incision was continued through the lid into the orbit. This permitted exploration of the orbit with the finger. About 1 cm. behind the orbital margin a sharp crest of bone could be felt running vertically down the orbital wall. Behind this crest no bone could be felt. The posterior part of the roof of the orbit was gone, and no bone could be felt in the region of the apex. As the patient lay on the operating table under colonic anesthesia, no pulsation of the right globe could be seen or felt, nor could pulsation be felt with the finger in the orbit.

On Jan. 8, 1932, an operation was performed to relieve the ptosis. Considerable skin and neoplastic tissue were removed, and an adjustment was made to correct the notch in the upper lid. Resection of the tarsus and the levator resulted in almost complete correction of the

ptosis. When the excised tissue was squeezed between the fingers, little papillae appeared which suggested the ends of small nerve trunks. The diagnosis of von Recklinghausen's disease was confirmed in the pathologic laboratory. This case is shown particularly to demonstrate visible pulsation of the right eye.

In the May, 1932, number of the *British Journal of Ophthalmology*. Dr. Foster Moore called attention to this phenomenon of pulsation and spoke of the possibility of its leading to the diagnosis of arteriovenous communication.

TWO CASES OF DISKLIKE MASSIVE EXUDATIVE DEGENERATION OF THE FOVEA. DR. RAYMOND PFEIFFER.

With an expression of the close similarity of the lesion to sarcoma of the choroid, and a sketch of the history of the disease from the first case reported by Michel in 1878, two cases of disciform degeneration of the fovea are presented. The first case is that of a man, 76 years old, with a lesion typical of the disease and affecting one eye, which has been observed for one year without noteworthy change. The second case is that of a man, aged 78, in whom the lesion occurs unilaterally and is associated with retinitis circinata which has been observed for four and one-half years without evident change in the elevated mass. Discussion of the pathologic process and differential diagnosis is omitted, a summary only being given. Both cases are illustrated with lantern slides.

DISCUSSION

DR. ERNST WALDSTEIN: There have appeared of late several articles in the German literature connecting the disklike degeneration of the macula and the angioid streaks (the latter condition is frequently associated with the former) with pseudoxanthoma elasticum Darier; the latter is a skin lesion characterized by brittleness and partial loss of the elastic fibers, and its co-appearance in certain regions of the body, as on the neck, above the clavicles and in the groins, with the two ocular disturbances mentioned above was first noted by Swedish authors in 1929. Up to the present time almost a dozen cases of such a co-existence of lesions in the fundus and the skin have been recorded. This occurrence is interesting in two respects: It explains the etiology of the angioid streaks, and the macular disciform degeneration, their prime cause being an alteration of the lamina vitrea of the choroid, and it opens a new outlook in a wide pathologic field, i. e., the reticulo-endothelial system, first disclosed by Aschoff. All the anomalies of lipoid metabolism can be brought in connection with the latter. I need not therefore emphasize its importance; may it suffice to mention Schueller-Christian's disease, morbus Gaucher and the large group of Niemann-Pick's diseases to which evidently amaurotic familial idiocy of Tay-Sachs and Wilson's pseudosclerosis (splenohepatomegalia) and probably also Hippel-Lindau's disease belong. One will, then, in the future have to look for some disease of the skin, at least in certain locations, when dealing with a number of interesting ocular conditions, especially of the fundus, which up to the present have defied analysis.

DR. CLYDE E. MCDANNALD: I should like to put on record two somewhat similar cases that I have seen: A man ten years ago came to

my office with bilateral lesions giving practically the same picture as in the first case shown here tonight. He was 70 years old; he had two white glistening spots in the macular area, elevated, without pigmentation and with no sign of inflammation. He gave a history of having had a carcinoma of the rectum removed about four years previously, but there seemed to be no particular connection between these two conditions.

The second patient has been under observation for the past two years. At present there is in the macular region of the right eye a large white noninflammatory elevated mass, slightly pigmented in its upper margin. This was seen to develop from what at first appeared to be a subhyaloid hemorrhage. Just now there exists in the left macular area an inflammatory state associated with hemorrhages which are coalescing, with the beginning formation of a white elevated mass, centrally situated. It is believed that a lesion similar to that seen in the right eye is developing. A thorough survey showed only some sclerosis of the retinal vessels without hypertension.

DR. FRANK CONRAD KEIL: I should like to ask Dr. Pfeiffer if this condition is not what the Germans and Viennese call Kuhnt-Junius disease. It often starts in one eye, but latter involves both eyes. There is one important point in diagnosis, that at times the condition is misinterpreted as a leukosarcoma. I saw one case at Professor Lindner's clinic where the physicians were very much in doubt. They waited, considering the diagnosis, until two years later the other eye became involved in the same way. The condition in that case was similar, discoid exudative retinitis.

DR. PERCY FRIEDENBERG: It strikes me that there is a little discrepancy between the fundus pictures in the two cases presented, and I think also on one point in the clinical history, I think that in these cases the condition is generally unilateral, as it was in Dr. Pfeiffer's first case. In the second case it is bilateral. All of us present saw a striking difference in the ophthalmoscopic pictures of the two cases. In the first case the condition was clinically discoid, but in the second case, it was not discoid at all. There was a large plaque, with a border of pigment, but there were also accessory lesions. There was definite arteriosclerosis. There was a circinate lesion deep in the retina, as well as a number of small hemorrhages. Does not that suggest more the condition that used to be called circinate retinitis and that is now known to be caused by sclerosis, and is not the second case distinguished from the first by the pigment? That suggests that it is possible that the two cases are not to be put in one pigeonhole.

DR. DAVID WEXLER: According to Verhoeff's description of Holloway's case of disklike degeneration at the macula, the lesion was a tumor-like mass of connective tissue situated behind the retina. The term should probably be restricted to cases in which such a mass is found on section. I believe that it is difficult accurately to distinguish the lesion from other exudative processes at the macula when they attain an unusual size.

DR. RAYMOND L. PFEIFFER: I think that the position of the vessels in both cases will indicate the position of the mass, which is not directly beneath the internal limiting membrane. This lesion is found associated

frequently with retinitis circinata; Junius and Kuhnt included three cases in their series. I have given a brief history of the disease. Had time permitted me to give my complete paper, many of these points would not have arisen.

Results Obtained by Modification of the Guist Operation for Detachment of the Retina. Dr. Hugh S. McKeown.

This paper will be published in full in a later issue of the Archives.

Isolation for Iris Prolapse. Dr. Rudolf Denig.

On the tenth day after a successful operation for cataract, the patient showed, as a result of a hemorrhage in the anterior chamber, a slight incarceration of the nasal pillar which was first considered negligible. About two weeks later, however, it had developed into a regular prolapse about half the size of a pea. As the eye became irritated and dangerous, excision of the prolapse then being out of the question, isolation was performed, with success. The operation consists in making a broad iridectomy on either side of the prolapsed or incarcerated iris. This procedure was described by Denig (*Klin. Monatsbl. f. Augenh.* **79:** 599, 1927). The eye and the prolapse have remained quiet ever since, although the latter, while shrunken to about one third of its original size, has not entirely flattened out. It can be abscised any time as Herman did (*Klin. Monatsbl. f. Augenh.* **87:** 845, 1931) who performed isolation and abscission at the same operation, but as there is no need for removal, because of the diminutive size and harmlessness of the prolapse, it should be let alone.

Lesions of the Fundus in the Malignant Phase of Essential Hypertension. Dr. Isadore Goldstein.

This paper will be published in full in a later issue of the Archives.

(*a*) A New Operation for Spastic Entropion. Dr. Julius Wolff.

(*b*) A New Operation on the Lids for Facial Paralysis. Dr. Julius Wolff.

The first procedure consisted of displacing the orbicularis from the lid margin. The second consisted of shortening and advancing the orbicularis at both canthi and fastening the ends to fixed points.

Book Reviews

Report of Government Ophthalmic Hospital, Madras, India, 1931. By Lt. Col. R. E. Wright, Superintendent. Price, 1 rupee, 6 annas. Pp. 54. Madras: Government Press, 1932.

During 1931, there were treated in this institution 3,923 inpatients and 28,831 outpatients; 5,969 operations were performed in the outpatient and inpatient departments, of which 1,816 were for senile cataract. Capsulotomy was performed in 1,518 cases; intracapsular operation (with forceps) in 14 cases; according to the Smith technic in 6 cases, and phaco-eresis (Barraquer) in 193 cases. Vitreous escape occurred in 33 cases (1.73 per cent), and iris prolapse in 15 (0.79 per cent). Colonel Wright believes that senile cataract is rare in India, and that the so-called nuclear cataract is the only form that should come under this heading, the bulk of the other types depending principally on defects in health.

Improvements in the performance of the operation for cataract are due to facial akinesia, which can now be obtained so satisfactorily by the O'Brien technic, and to deep orbital injection in the region of the ciliary ganglion. There remain the three following problems: (1) the embarrassment of blood entering the anterior chamber at the time of operation; (2) the certain attainment of a large central gap in the anterior capsule; (3) the method of securing the section.

Colonel Wright believes that the hemorrhage in the anterior chamber is the greatest difficulty in the capsulotomy procedure and that it is the greatest drawback to the bridge flap method of cataract extraction; blood and cortex facilitate the formation of after-cataracts and are liable to set up an iritis and to make the operation on the after-cataract more difficult. It seems that Indian eyes are much more prone to hemorrhage in the anterior chamber than American or European eyes, and, curiously enough, the Indian eye responds poorly to mydriatics, such as atropine, cocaine or epinephrine. This, Colonel Wright thinks, is due to the fact that the deeply pigmented iris is more rigid and to the frequent association with hyperglycemia. He is inclined to revert to the old technic of section just short of the corneal-scleral junction in order to insure a bloodless operation, though he regrets losing the advantage of a flap.

After trying every known method for procuring a large central aperture in the anterior capsule, Colonel Wright has finally returned to an old procedure in which a large tongue-shaped flap in the capsule is executed with the knife at the time of making the section. This is subsequently torn off with the forceps. The method of preliminary capsulotomy which has been practiced in Madras for about a century has many advantages, especially in dealing with complicated cases. The difficulties that are presented by a small, rigid pupil must be kept in mind by operators in India.

Looking back on an experience of 20,000 odd cataract extractions, Colonel Wright discusses the various methods of intracapsular operation: the Smith expression, the extraction with capsule forceps and the

Barraquer procedure, giving their advantages and their difficulties. He does not think that the piece of capsule obtained in the attempt to dislocate the lens with the forceps when the capsule ruptures is as satisfactory as would be the result from a capsulotomy done for that purpose alone. In brief, he practices the intracapsular operation when this procedure is suitable and the casulotomy method in the remaining 50 per cent of the cases.

One hundred and nineteen trephining operations were performed for glaucoma. The Lagrange method was performed three times, and another attempt was made to try out iridencleisis. The objection that the author has to this procedure is that it is suitable only to patients who are get-at-able, and he reports the case of a patient on whom iridencleisis was performed without any untoward event, but on the sixth day a severe attack of acute congestive glaucoma developed.

In the Madras Clinic glaucoma is frequently due to intumescent and hypermature cataracts. Colonel Wright divides these cases under the following headings: (1) secondary glaucoma due to swelling of the lens (without a trace of iritis); (2) secondary glaucoma due to irritation of morgagnian fluid, and (3) a combination of the two.

In acute secondary glaucoma an attempt is made to reduce the tension with physostigmine (eserine), leeches, purgation, morphine and epinephrine packs, and then to do a broad iridectomy. This generally gives satisfactory results, and the extraction can then be done after two weeks. In cases of acute glaucoma in hypermature cataracts, Colonel Wright thinks that the glaucoma is due to a seeping of the irritating morgagnian fluid, and the eye shows definite evidences of irritative phacogenetic iritis.

The alimentary canal as a source of ocular trouble has been given considerable attention in the Madras Clinic, and Colonel Wright thinks that certain types of quiet iritis of unknown etiology have their origin in the alimentary tract. Though this iritis seems to have no characteristic signs, nevertheless, treatment of the alimentary canal is of benefit in certain cases, and the author recommends it particularly in cases in which the usual factors have been excluded. The patient is given large quantities of saline water to drink, until the salt solution comes through practically clean.

During 1931, superficial punctate keratitis continued in an epidemic form. Colonel Wright prefers the term keratitis diversiformis and uveitis anterior. The various forms in which this disease has appeared were described in the *British Journal of Ophthalmology* in June and November, 1930.

Many other instructive and interesting conditions are described which give evidence of the vast opportunities the Madras institution offers and which are so admirably taken advantage of by the present director.

A fitting conclusion to this important report is a historical survey of the Government Ophthalmic Hospital in Madras. The clinic apparently was organized about 1819, by Mr. R. Richardson, one of the East India Company surgeons. He was succeeded by Lane, Thompson, Shaw, Hall, Smith, Chipperfield, Furnell, Brockman, Pope, Elliot, Kirkpatrick and the present superintendent.

A. K.

Zur Behandlung der Netzhautablösung mittels Diathermie. By Prof. H. Weve, Utrecht. Supplement to Zeitschrift für Augenheilkunde. Price, 3 marks. Pp. 49, with 24 illustrations. Berlin: S. Karger, 1932.

Some years ago the author reported on the closure of the tear in retinal detachment with diathermy, and in May, 1931, some of the patients who had been cured were demonstrated before the Netherland Ophthalmological Society.

A similar method was independently suggested by Larson, but this last author does not insist on directly treating the retinal tear. Weve is convinced that endothermy has a future in ophthalmology in general and in the treatment of retinal detachment in particular, where it is applied by either a broad surface adhesion or a multiple micropuncture surrounding the tear in the retina.

Weve uses the Gonin procedure in cases in which this method can be easily followed out with promising results, but in cases with extensive peripheric separations and tears diathermy has given the best results.

In this operation the apparatus of Monbrun and Casteran (manufactured by Walter in Paris) is used, which permits the exact measurement of slight intensities. The cuff consists of a tin surface which is applied to the arm. For surface treatment, the active electrode is a needle with a metal button from 3 to 5 mm. in diameter, while fine needles are used in the encircling method. The conjunctival wound is held open with glass hooks or spoons. The scleral surface must be kept dry. The electrode, after sterilization, is applied to the sclera, and the current is closed through the foot control. The current must not be stronger than 150 ma. for the button electrode, which is applied until the sclera appears dried out and discolored. This is repeated a few millimeters distant, until the affected area is circled. If the retina is not in approximate contact, a small puncture is made to let off the subretinal fluid; otherwise, the eyeball is not opened. After the operation, the patient is placed just as in the Gonin operation, with the tear most dependent. On the third or fourth day, the intra-ocular pressure is found much reduced, but after a week improvement is definitely present. The heated area at first appears as a snow-white discoloration of the retina, and the changes in the pigment which follow the cicatrization extend but little beyond the treated area.

When the tear is more centrally located, the needle electrode is applied in a circle or curve about the tear and introduced for one-third the scleral thickness with a current intensity of 50 ma. A number of perforations are made to let off the fluid.

Up to the end of 1931, twenty-three patients were treated with surface diathermy. In eleven, permanent reattachment took place. In some cases a partial result was obtained. No permanent result was obtained in eleven cases. A cataract subsequently (after from one to one and a half years) developed in four cases. The case histories are then described in detail and must be carefully studied.

In this, as in all other methods of treatment, there are favorable and unfavorable cases. To try out his method, Weve operated in all cases, especially in those not suited for the Gonin operation or in which the latter method had failed. In general, the results are best in youthful

nonmyopic eyes, especially with ora tears, and the technic is surely much simpler than the Guist. The eyeball was not perforated in most cases, and there were no vitreous hemorrhages, though the possibility of cataract must be borne in mind.

Weve's and Larsson's method is a most important contribution and represents a promising advance in the operative treatment of retinal detachment.

A. K.

Collected Reprints from the Wilmer Ophthalmological Institute of the Johns Hopkins University and Hospital. Volume II, 1930-1931, inclusive. Baltimore, 1932.

This volume contains forty-seven reprints of publications by the members of the Wilmer Institute, which were published in various journals during 1930 and 1931, and the titles of five publications that are not reprinted. These were written by the director, Dr. William H. Wilmer, and Dr. A. C. Woods, Dr. Jonas S. Friedenwald, Professors Ferree and Rand and a few others.

This imposing volume brings together a wide variety of subjects that bear testimony to the many-sided and excellent work being done at the Institute.

Directory of Ophthalmologic Societies *

INTERNATIONAL

International Association for Prevention of Blindness

President: Prof. F. de Lapersonne, 217, Faubourg St. Honoré, Paris.
Secretary-General pro tem: Dr. A. Churchill, 66, Boulevard St. Michel, Paris.

International Ophthalmologic Congress

Secretary: Dr. Franciso Poyales, Olozaga 3, Madrid, Spain.
Place: Madrid, Spain. Time, April 16-22, 1933.

FOREIGN

British Medical Association, Section on Ophthalmology

President: Sir J. Herbert Parsons, 54 Queen Anne St., Cavendish Square, London, W. I.

Ophthalmological Society of the United Kingdom

President: Mr. A. H. H. Sinclair, 6 Charlotte Square, Edinburgh.
Secretary: Mr. Humphrey Neame, 56 Portland Place, London, W. I.

Oxford Ophthalmological Congress

Master: Dr. Cyril Walker, Bristol, England.
Secretary: Dr. C. G. Russ-Wood, 12 St. John's Hill, Shrewsbury, England.

Royal Society of Medicine, Section of Ophthalmology

President: Dr. E. W. Brewerton, 73 Harley St., W. 1, London.
Secretary: Dr. P. G. Doyne, 60 Queen Anne St., W. 1, London.

Société Française d'Ophthalmologie

Secretary: Dr. René Onfray, 6 avenue de la Motte Picquet, Paris 7è.

German Ophthalmological Society

Secretary: Prof. A. Wagenmann, Heidelberg.

NATIONAL

American Medical Association, Section on Ophthalmology

Chairman: Dr. Frederick H. Verhoeff, 82 Commonwealth Ave., Boston.
Secretary: Dr. Parker Heath, 1551 Woodward Ave., Detroit.
Place: Milwaukee. Time: June 12-16, 1933.

American Academy of Ophthalmology and Oto-Laryngology

President: Dr. S. Hanford McKee, 1528 Crescent St., Montreal, Canada.
President-Elect: Dr. B. R. Shurley, 62 W. Adams Ave., Detroit.
Executive Secretary: Dr. William P. Wherry, Medical Arts Bldg., Omaha.
Place: Montreal, Canada. Time: September 19-23, 1932.

American Ophthalmological Society

President: Dr. Edward C. Ellett, 130 Madison Ave., Memphis, Tenn.
Secretary: Dr. Emory Hill, Professional Bldg., Richmond, Va.

SECTIONAL

New England Ophthalmological Society

President: Dr. David W. Wells, Hotel Westminster, Boston.
Secretary-Treasurer: Dr. Theodore L. Terry, 243 Charles St., Boston.
Place: Massachusetts Eye and Ear Infirmary, 243 Charles St., Boston. Time: 8 p. m., third Tuesday of each month from November to April, inclusive.

* Secretaries of societies are requested to furnish the information necessary to make this list complete and to keep it up to date.

Pacific Coast Oto-Ophthalmological Society

President: Dr. Hans Barkan, 490 Post St., San Francisco.
Secretary-Treasurer: Dr. J. Frank Friesen, 1208 Roosevelt Bldg., Los Angeles.
Place: San Francisco. Time: 1933.

Puget Sound Academy of Ophthalmology and Oto-Laryngology

President: Dr. John H. Harter, 1215 Fourth Ave., Seattle.
Secretary-Treasurer: Dr. Francis A. Brugman, 806 Cobb Bldg., Seattle.
Time: 8 p. m., third Tuesday of each month, except July and August.

Saginaw Valley Academy of Ophthalmology and Otolaryngology

President: Dr. R. B. Smith, Alma, Mich.
Secretary-Treasurer: Dr. W. K. Slack, 308 Eddy Bldg., Saginaw, Mich.
Place: Saginaw, Mich., or Bay City, Mich. Time: First Friday of each month, except July and August.

Sioux Valley Eye and Ear Academy

President: Dr. John B. Gregg, 101 S. Main St., Sioux Falls, S. Dakota.
Secretary-Treasurer: Dr. F. H. Roost, 420 Trimble Bldg., Sioux City, Iowa.
Place: Sioux City, Iowa. Time: November, 1932.

Southern Medical Association, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Wiley R. Buffington, 211 Camp St., New Orleans.
Secretary: Dr. William D. Gill, 323 Medical Arts Bldg., San Antonio, Texas.
Place: Birmingham, Ala. Time: November, 1932.

Southwestern Michigan Triological Society

President: Dr. W. E. McGarvey, 802 Jackson City Bank Bldg., Jackson.
Secretary: Dr. Don C. Lyons, 1405 Union and Peoples National Bank Bldg., Jackson.
Time: Third Thursday of alternate months.

STATE

Colorado Ophthalmological Society

President: A presiding officer is selected for each meeting alternatelv until all members have served.
Secretary: Dr. Ralph W. Danielson, 258 Metropolitan Bldg., Denver.
Place: Capitol Life Building, Denver. Time: 7:30 p. m., third Saturday of the month, October to April, inclusive.

Connecticut State Medical Society, Section on Eye, Ear, Nose and Throat

President: Dr. M. H. Gill, 36 Pearl St., Hartford.
Secretary-Treasurer: Dr. Walter L. Hogan, 750 Main St., Hartford.
Time: May, November.

Eye, Ear, Nose and Throat Club of Georgia

President: Dr. Thomas H. Hall, Jr., 617 Mulberry St., Macon.
Secretary-Treasurer: Dr. J. A. Smith, 700 Spring St., Macon.

Indiana Academy of Ophthalmology and Oto-laryngology

President: Dr. J. R. Gillum, 221 S. Sixth St., Terre Haute.
Secretary: Dr. J. Kent Leasure, 23 E. Ohio St., Indianapolis.

Iowa Academy of Ophthalmology and Oto-Laryngology

President: Dr. Royal French, 28 S. First Ave., Marshalltown.
Secretary-Treasurer: Dr. W. F. Boiler, 105 E. Iowa Ave., Iowa City.

MICHIGAN STATE MEDICAL SOCIETY, SECTION OF OPHTHALMOLOGY AND OTOLARYNGOLOGY

Chairman: Dr. Wilfred Haughey, 303 Post Bldg., Battle Creek.
Secretary: Dr. H. O. Westervelt, 239 Pipestone St., Benton Harbor.

MINNESOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Douglas F. Wood, 74 S. Ninth St., Minneapolis.
Secretary-Treasurer: Dr. Walter E. Camp, Medical Arts Bldg., Minneapolis.
Time: Second Friday of each month from October to May.

MONTANA ACADEMY OF OTO-OPHTHALMOLOGY

President: Dr. L. H. Huber, Livingston.
Secretary: Dr. A. W. Morse, Phoenix Bldg., Butte.

NEW JERSEY STATE MEDICAL SOCIETY, SECTION ON OPHTHALMOLOGY, OTOLOGY AND RHINOLARYNGOLOGY

Chairman: Dr. Charles H. Schlichter, 556 N. Broad St., Elizabeth.
Secretary: Dr. B. E. Failing, 31 Lincoln Park, Newark.

NEW YORK STATE MEDICAL SOCIETY, EYE, EAR, NOSE AND THROAT SECTION

Chairman: Dr. D. F. Gillette, 109 S. Warren St., Syracuse.
Secretary: Dr. Frank M. Sulzman, 1831 Fifth Ave., Troy.

NORTH DAKOTA ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. Axel Oftedal, 55½ Broadway, Fargo.
Secretary-Treasurer: Dr. F. L. Wicks, 516 Fourth St., Valley City.

OREGON ACADEMY OF OPHTHALMOLOGY AND OTO-LARYNGOLOGY

President: Dr. H. M. Hendershott, 193 Eleventh St., Portland.
Secretary-Treasurer: Dr. Andrew J. Browning, 418 Mayer Bldg., Portland.
Place: Good Samaritan Hospital. Time: Third Tuesday of each month.

RHODE ISLAND OPHTHALMOLOGICAL AND OTOLOGICAL SOCIETY

President: Dr. Herman A. Winkler, 224 Thayer St., Providence.
Secretary: Dr. N. A. Bolotow, 108 Waterman St., Providence.
Place: Rhode Island Medical Library. Time: 8:30 p. m., second Thursday in October, December, February and April.

SOUTH CAROLINA MEDICAL ASSOCIATION, SECTION ON OPHTHALMOLOGY AND OTOLARYNGOLOGY

President: Dr. W. B. McWhorter, 106 E. Earle St., Anderson.
Secretary-Treasurer: Dr. G. M. Truluck, Orangeburg.
Time: April and December.

TEXAS OPHTHALMOLOGICAL AND OTO-LARYNGOLOGICAL SOCIETY

President: Dr. W. D. Jones, 3116 Live Oak St., Dallas, Texas.
Secretary: Dr. A. F. Clark, 1034 Nix Professional Bldg., San Antonio.

UTAH OPHTHALMOLOGICAL SOCIETY

President: Dr. D. W. Henderson, 75 S. Main St., Salt Lake City.
Secretary-Treasurer: Dr. T. F. Welch, 14 Exchange Pl., Salt Lake City.

VIRGINIA SOCIETY OF OTO-LARYNGOLOGY AND OPHTHALMOLOGY

President: Dr. Frank P. Swart, 142 W. York St., Norfolk.
Secretary-Treasurer: Dr. H. G. Preston, 307 Professional Bldg., Harrisonburg.

WEST VIRGINIA STATE MEDICAL ASSOCIATION, EYE, EAR, NOSE AND THROAT SECTION

President: Dr. O. H. Bobbitt, Medical Arts Bldg., Charleston.
Secretary: Dr. Harry V. Thomas, 95 Fairmont Ave., Fairmont.

LOCAL

Academy of Medicine of Northern New Jersey, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Elbert A. Curtis, 65 Central St., Newark.
Secretary: Dr. A. Russell Sherman, 671 Broad St., Newark.
Place: 91 Lincoln Park South. Time: 8:45 p. m., second Monday of each month.

Academy of Medicine of Toronto, Section of Ophthalmology

Chairman: Dr. P. J. F. Houston, 34 Hurndale Ave., Toronto.
Secretary: Dr. Alexander E. MacDonald, 151 Bloor St., W., Toronto.
Time: First Monday of winter months.

Atlanta Eye, Ear, Nose and Throat Society

President: Dr. L. C. Rouglin, 127 Peachtree St., N. E., Atlanta, Ga.
Secretary: Dr. William O. Martin, Jr., Medical Arts Bldg., Atlanta, Ga.
Place: Academy of Medicine, 38 Prescott St., N. E. Time: 8 p. m., last Thursday of each month.

Baltimore Medical Society, Section on Ophthalmology

Chairman: Dr. Harry Friedenwald, 1212 Eutaw Pl., Baltimore.
Secretary: Dr. William M. Rowland, 906 Cathedral St., Baltimore.
Place: Medical and Chirurgical Faculty, 1211 Cathedral St. Time: 8:30 p. m., fourth Thursday of each month from October to May.

Brooklyn Ophthalmological Society

President: Dr. W. F. C. Steinbugler, 515 Ocean Ave., Brooklyn.
Secretary: Dr. Walter V. Moore, 1 Nevins St., Brooklyn.
Place: Kings County Medical Society Bldg., 1313 Bedford Ave. Time: Third Thursday in February, April, May, October and December.

Buffalo Ophthalmologic Club

President: Dr. H. D. Andrews, 33 Allen St., Buffalo.
Secretary-Treasurer: Dr. Thurber Le-Win, 112 Linwood Ave., Buffalo.

Chicago Ophthalmological Society

President: Dr. Frank Brawley, 30 N. Michigan Ave., Chicago.
Secretary: Dr. Richard C. Gamble, 30 N. Michigan Ave., Chicago.
Place: Medical and Dental Arts Club. Time: Third Monday of each month from October to May.

Cleveland Academy of Medicine, Section of Ophthalmology and Oto-Laryngology

Chairman: Dr. M. W. Jacoby, 2323 Prospect Ave., Cleveland.
Secretary: Dr. H. C. Rosenberger, 1065 Rose Bldg., Cleveland.
Place: Winton Hotel. Time: Fourth Friday of each month.

Cleveland Ophthalmological Club

Chairman: Dr. Roy B. Metz, Hanna Bldg., Cleveland.
Secretary: Dr. Paul G. Moore, Medical Arts Bldg., Cleveland.

College of Physicians, Philadelphia, Section on Ophthalmology

Chairman: Dr. L. F. Appleman, 308 S. Sixteenth St., Philadelphia.
Clerk: Dr. Alexander G. Fewell, 1924 Pine St., Philadelphia.
Time: Third Thursday of every month from October to April, inclusive.

Columbus Ophthalmological and Oto-Laryngological Society

Chairman: Dr. John B. Alcorn, 167 E. State St., Columbus, Ohio.
Secretary-Treasurer: Dr. Edward W. Harris, 681 E. Broad St., Columbus, Ohio.
Time: First Monday of each month.

Dallas Academy of Ophthalmology and Oto-Laryngology

President: Dr. O. M. Marchman, 1717 Pacific Ave., Dallas, Texas.
Recording Secretary: Dr. W. Mood Knowles, 1717 Pacific Ave., Dallas, Texas.
Corresponding Secretary: Dr. J. M. Potts, 1717 Pacific Ave., Dallas, Texas.
Place: Dallas Athletic Club. Time: 6:30 p. m., first Tuesday of each month from October to June. The November, January and March meetings are devoted to clinical work.

Des Moines Academy of Ophthalmology and Otolaryngology

President: Dr. Cecil C. Jones, 1121 Equitable Bldg., Des Moines, Iowa.
Secretary-Treasurer: Dr. Grace Doane, 614 Bankers Trust Bldg., Des Moines, Iowa.
Time: 7:45 p. m., third Monday of every month, September to May.

Detroit Ophthalmological Club

Chairman: Members rotate alphabetically.
Secretary: Dr. Raymond S. Goux, David Whitney Bldg., Detroit.
Time: 6:30 p. m., first Wednesday of each month.

Eastern New York Eye, Ear, Nose and Throat Association

President: Dr. R. H. Seeley, 9 Court St., Rutland, Vt.
Secretary-Treasurer: Dr. Arthur F. Holding, 142 Washington Ave., Albany.
Time: Third Wednesday in October, November, March, April, May and June.

Fort Worth Eye, Ear, Nose and Throat Society

President: Dr. R. H. Needham, 1304 Medical Arts Bldg., Fort Worth, Texas.
Secretary-Treasurer: Dr. Van D. Rathgeber, 1011 Medical Arts Bldg., Fort Worth.
Place: University Club. Time: 6:30 p. m., first Friday of each month except July and August.

Grand Rapids Eye, Ear, Nose and Throat Society

President: Dr. Carl F. Snapp, 26 Sheldon Ave., Grand Rapids, Mich.
Secretary-Treasurer: Dr. Walter W. Oliver, 26 Sheldon Ave., Grand Rapids, Mich.
Place: Various local hospitals. Time: Third Thursday of alternating months, September to May.

Houston Academy of Medicine, Eye, Ear, Nose and Throat Section

President: Dr. L. W. Raney, 609 Fannin St., Houston, Texas.
Secretary: Dr. J. F. Gamble, 201 Main St., Houston, Texas.
Place: Medical Arts Bldg., Harris County Medical Society Rooms. Time: 8 p. m., first Thursday of each month from September to June.

Indianapolis Ophthalmological and Oto-Laryngological Society

President: Dr. John W. Carmack, 23 E. Ohio St., Indianapolis.
Secretary: Dr. Kenneth L. Craft, 23 E. Ohio St., Indianapolis.
Place: University Club. Time: 6:30 p. m., second Thursday of each month from October to May.

Kansas City Society of Ophthalmology and Oto-Laryngology

President: Dr. Albert N. Lemoine, 906 Grand Ave. ,Kansas City, Mo.
Secretary: Dr. Harold B. Hedrick, 618 Professional Bldg., Kansas City, Mo.
Time: Third Thursday of each month from September to May. The November, January and March meetings are devoted to clinical work.

Long Beach Eye, Ear, Nose and Throat Society

President: Dr. Ferris L. Arnold, 923 Security Bldg., Long Beach, Calif.
Secretary-Treasurer: Dr. Clyde E. Harner, 312 Security Bldg., Long Beach, Calif.
Place: Professional Bldg. Time: Last Wednesday of each month from September to June.

Los Angeles County Medical Society, Section on Ophthalmology and Oto-Laryngology

President: Dr. J. Frank Friesen, 1208 Roosevelt Bldg., Los Angeles.
Secretary-Treasurer: Dr. F. H. Brandt, 1052 W. Sixth St., Los Angeles.
Place: Mary Louise Cafe. Time: 6:30 p. m., fourth Monday of each month from October to May, inclusive.

Medical Society of the District of Columbia, Section of Ophthalmology and Oto-Laryngology

Chairman: Dr. Albert P. Tibbets, 1801 I St., Washington.
Secretary Dr. G. Victor Simpson, Rhode Island Ave., Washington.
Place: 1718 M St., N. W. Time: 8 p. m., third Friday of each month from October to April, inclusive.

Memphis Society of Ophthalmology and Oto-Laryngology

Chairman: Each member, in alphabetical order.
Secretary: Dr. R. O. Rychener, Exchange Bldg., Memphis, Tenn.
Place: Eye Clinic of Memphis Eye, Ear, Nose and Throat Hospital. Time: 8 p. m., second Tuesday of each month. Annual meeting, Jan. 10, 1933.

Milwaukee Oto-Ophthalmic Society

President: Dr. T. F. McCormick, 324 Wisconsin Ave., Milwaukee.
Secretary-Treasurer: Dr. O. P. Schoofs, 324 E. Wisconsin Ave., Milwaukee.
Place: University Club. Time: 6:30 p. m., third Tuesday of each month.

Montreal Ophthalmological Society

President: Dr. J. P. E. Bousquet, 66 Sherbrooke St., West, Montreal, Canada.
Secretary: Dr. J. A. MacMillan, 1410 Stanley St., Montreal, Canada.
Time: Second Thursday of October, December, February and April.

Nashville Academy of Ophthalmology and Otolaryngology

Chairman: Dr. Hilliard Wood, 700 Church St., Nashville, Tenn.
Secretary-Treasurer: Dr. H. C. Smith, Medical Arts Bldg., Nashville, Tenn.
Place: St. Thomas Hospital. Time: 8 p. m., third Monday of each month.

New Orleans Ophthalmological and Otolaryngological Society

President: Dr. Charles A. Bahn, 150 Baronne St., New Orleans.
Secretary-Treasurer: Dr. M. F. Meyer, Canal Bank Bldg., New Orleans.
Place: Eye, Ear, Nose and Throat Hospital. Time: Third Thursday of each month from October to June.

New York Academy of Medicine, Section of Ophthalmology

Chairman: Dr. Mark J. Schoenberg, 1160 Park Ave., New York.
Secretary: Dr. Algernon B. Reese, 73 E. Seventy-First St., New York.
Time: 8:30 p. m., third Monday of every month from October to May, inclusive.

Omaha and Council Bluffs Ophthalmological and Oto-Laryngological Society

President: Dr. L. G. Howard, 532 First Ave., Council Bluffs, Iowa.
Secretary-Treasurer: Dr. W. A. Cassidy, 1620 Medical Arts Bldg., Omaha.
Place: Omaha Club, 20th and Douglas Sts., Omaha. Time: 6 p. m., dinner; 7 p. m., program; third Wednesday of each month from October to May.

Pittsburgh Ophthalmological Society

President: Dr. Edward B. Heckel, Jenkins Arcade Bldg., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: Pittsburgh Academy of Medicine Bldg. Time: Fourth Monday of each month, except June, July, August and September.

Pittsburgh Slit-Lamp Society

President: Dr. W. W. Blair, 121 University Pl., Pittsburgh.
Secretary: Dr. George H. Shuman, Park Bldg., Pittsburgh.
Place: 121 University Pl. Time: Second Monday evening of every month, except June, July, August and September.

Richmond Ophthalmological and Oto-Laryngological Society

President: Dr. William R. Weisiger, Medical Arts Bldg., Richmond, Va.
Secretary: Dr. R. W. Vaughan, Medical Arts Bldg., Richmond, Va.
Place: Westmoreland Club. Time: 6 p. m., second Monday of each month from October to May.

Rochester Eye, Ear, Nose and Throat Society

Chairman: Dr. E. S. Amsler, 53 S. Fitzhugh St., Rochester, N. Y.
Secretary-Treasurer: Dr. E. W. O'Brien, 5 N. Goodman St., Rochester, N. Y.
Place: Rochester Medical Association, 113 Prince St. Time: 8 p. m., third Monday of each month from October to May.

St. Louis Ophthalmic Society

President: Dr. Julius H. Gross, Carleton Bldg., St. Louis.
Secretary: Dr. Carl T. Eber, 1006 Carleton Bldg., St. Louis.
Place: Oscar Johnson Institute. Time: Clinical meeting 5:30 p. m., dinner and scientific meeting 6:30 p. m., fourth Friday of each month from October to April, inclusive, except December.

San Antonio Ophthalmolo-Oto-Laryngological Society

President: Dr. Charles J. Boehs, Medical Arts Bldg., San Antonio, Texas.
Secretary-Treasurer: Dr. E. D. Dumas, 425 Medical Arts Bldg., San Antonio, Texas.
Place: Bexar County Medical Library. Time: 8 p. m., first Tuesday of each month from October to May.

San Francisco County Medical Society, Section on Eye, Ear, Nose and Throat

Chairman: Dr. Robert C. Martin, 384 Post St., San Francisco.
Secretary: Dr. George N. Hosford, 490 Post St., San Francisco.
Place: Society's Building, 2180 Washington St., San Francisco.
Time: Third Tuesday of every month except May, June, July and December.

Shreveport Eye, Ear, Nose and Throat Society

President: Dr. J. L. Scales, Medical Arts Bldg., Shreveport, La.
Secretary-Treasurer: Dr. W. L. Atkins, 505 Medical Bldg., Shreveport, La.
Place: 1240 Texas Ave. Time: 7:30 p. m., first Monday of each month from October to June.

Spokane Academy of Ophthalmology and Oto-Laryngology

President: Dr. David Hartin, Old National Bank Bldg., Spokane, Wash.
Secretary: Dr. W. W. Henderson, Paulsen Medical and Dental Bldg., Spokane, Wash.
Place: Paulsen Medical and Dental Library. Time: 8 p. m., fourth Tuesday of each month except June, July and August.

Syracuse Eye, Ear, Nose and Throat Society

President: Dr. W. G. Dickinson, 504 State Tower Bldg., Syracuse, N. Y.
Secretary-Treasurer: Dr. Harold H. Joy, 504 State Tower Bldg., Syracuse, N. Y. N. Y.
Place: University Club. Time: Second Friday of each month except June, July and August.

Tulsa Academy of Ophthalmology and Otolaryngology

President: Dr. Roy Dunlap, 108 W. Sixth St., Tulsa, Okla.
Secretary-Treasurer: Dr. Marvin D. Henley, 108 W. Sixth St., Tulsa, Okla.
Place: Medical Arts Bldg. Time: Monthly.